

SOLUTIONS MANUAL

Jan William Simek



ORGANIC CHEMISTRY

SIXTH EDITION

L. G. Wade, Jr.



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California Polytechnic State University

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PREFACE

Hints for Passing Organic Chemistry

Do you want to pass your course in organic chemistry? Here is my best advice, based on over thirty years of observing students learning organic chemistry:

Hint #1: *Do the problems.* It seems straightforward, but humans, including students, try to take the easy way out until they discover there is no short-cut. Unless you have a measured IQ above 200 and comfortably cruise in the top 1% of your class, *do the problems*. Usually your teacher (professor or teaching assistant) will recommend certain ones; try to do all those recommended. If you do half of them, you will be half-prepared at test time. (Do you want your surgeon coming to your appendectomy having practiced only *half* the procedure?) And when you do the problems, keep this Solutions Manual CLOSED. Avoid looking at *my* answer before you write *your* answer—your trying and struggling with the problem is the most valuable part of the problem. Discovery is a major part of learning. Remember that the primary goal of doing these problems is *not* just getting the right answer, but understanding the material well enough to get right answers to the questions you haven't seen yet.

Hint #2: *Keep up.* Getting behind in your work in a course that moves as quickly as this one is the Kiss of Death. For most students, organic chemistry is the most rigorous intellectual challenge they have faced so far in their studies. Some are taken by surprise at the diligence it requires. Don't think that you can study all of the material the couple of days before the exam—well, you can, but you won't pass. Study organic chemistry like a foreign language: try to do some every day so that the freshly-trained neurons stay sharp.

Hint #3: *Get help when you need it.* Use your teacher's office hours when you have difficulty. Many schools have tutoring centers (in which organic chemistry is a popular offering). Here's a secret: absolutely the best way to cement this material in your brain is to get together with a few of your fellow students and make up problems for each other, then correct and discuss them. When *you* write the problems, you will gain great insight into what this is all about.

Purpose of this Solutions Manual

So what is the point of this Solutions Manual? First, I can't do your studying for you. Second, since I am not leaning over your shoulder as you write your answers, I can't give you direct feedback on what you write and think—the print medium is limited in its usefulness. What I *can* do for you is: 1) provide correct answers; the publishers, Professor Wade, Professor Kantorowski (my reviewer), and I have gone to great lengths to assure that what I have written is correct, for we all understand how it can shake a student's confidence to discover that the answer book flubbed up; 2) provide a considerable degree of rigor; beyond the fundamental requirement of correctness, I have tried to flesh out these answers, being complete but succinct; 3) provide insight into how to solve a problem and into where the sticky intellectual points are. Insight is the toughest to accomplish, but over the years, I have come to understand where students have trouble, so I have tried to anticipate your questions and to add enough detail so that the concept, as well as the answer, is clear.

It is difficult for students to understand or acknowledge that their teachers are human (some are more human than others). Since I am human (despite what my students might report), I can and do make mistakes. If there are mistakes in this book, they are my sole responsibility, and I am sorry. If you find one, PLEASE let me know so that it can be corrected in future printings. Nip it in the bud.

What's New in this edition?

Better answers! Part of my goal in this edition has been to add more explanatory material to clarify how to arrive at the answer. The possibility of more than one answer to a problem has been noted. The IUPAC Nomenclature appendix has been expanded to include bicyclics, heteroatom replacements, and the Cahn-Ingold-Prelog system of stereochemical designation.

Better graphics! The print medium is very limited in its ability to convey three-dimensional structural information, a problem that has plagued organic chemists for over a century. I have added some graphics created in the software, Chem3D®, to try to show atoms in space where that information is a key part of the solution. In drawing NMR spectra, representational line drawings have replaced rudimentary attempts at drawing peaks from previous editions.

Better jokes? Too much to hope for.

Some Web Stuff

Prentice-Hall maintains a web site dedicated to the Wade text: try www.prenhall.com/wade. Two essential web sites providing spectra are listed on the bottom of p. 270.

Acknowledgments

No project of this scope is ever done alone. These are team efforts, and there are several people who have assisted and facilitated in one fashion or another who deserve my thanks.

Professor L. G. Wade, Jr., your textbook author, is a remarkable person. He has gone to extraordinary lengths to make the textbook as clear, organized, informative and insightful as possible. He has solicited and followed my suggestions on his text, and his comments on my solutions have been perceptive and valuable. We agreed early on that our primary goal is to help the students learn a fascinating and challenging subject, and all of our efforts have been directed toward that goal. I have appreciated our collaboration.

My new colleague, Dr. Eric Kantorowski, has reviewed the entire manuscript for accuracy and style. His diligence, attention to detail and chemical wisdom have made this a better manual. Eric stands on the shoulders of previous reviewers who scoured earlier editions for errors: Jessica Gilman, Dr. Kristen Meisenheimer, and Dr. Dan Mattern. Mr. Richard King has offered numerous suggestions on how to clarify murky explanations. I am grateful to them all.

The people at Prentice-Hall have made this project possible. Good books would not exist without their dedication, professionalism, and experience. Among the many people who contributed are: Lee Englander, who connected me with this project; Nicole Folchetti, Advanced Chemistry Editor; and Kristen Kaiser and Carole Snyder, Project Managers.

The entire manuscript was produced using *ChemDraw*®, the remarkable software for drawing chemical structures developed by CambridgeSoft Corp., Cambridge, MA. We, the users of sophisticated software like ChemDraw, are the beneficiaries of the intelligence and creativity of the people in the computer industry. We are fortunate that they are so smart.

Finally, I appreciate my friends who supported me throughout this project, most notably my good friend of almost forty years, Judy Lang. The students are too numerous to list, but it is for them that all this happens.

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DEDICATION

To my inspirational chemistry teachers:

Joe Plaskas, who made the batter;

Kurt Kaufman, who baked the cake;

Carl Djerassi, who put on the icing;

and to my parents:

Ervin J. and Imilda B. Simek,

who had the original concept.

SYMBOLS AND ABBREVIATIONS

Below is a list of symbols and abbreviations used in this Solutions Manual, consistent with those used in the textbook by Wade. (Do not expect all of these to make sense to you now. You will learn them throughout your study of organic chemistry.)

BONDS

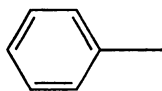
	a single bond
	a double bond
	a triple bond
	a bond in three dimensions, coming out of the paper toward the reader
	a bond in three dimensions, going behind the paper away from the reader
	a stretched bond, in the process of forming or breaking

ARROWS

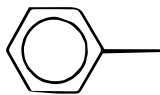
	in a reaction, shows direction from reactants to products
	signifies equilibrium (not to be confused with resonance)
	signifies resonance (not to be confused with equilibrium)
	shows direction of electron movement: the arrowhead with one barb shows movement of one electron; the arrowhead with two barbs shows movement of a pair of electrons
	shows polarity of a bond or molecule, the arrowhead signifying the more negative end of the dipole

SUBSTITUENT GROUPS

Me	a methyl group, CH ₃
Et	an ethyl group, CH ₂ CH ₃
Pr	a propyl group, a three carbon group (two possible arrangements)
Bu	a butyl group, a four carbon group (four possible arrangements)
R	the general abbreviation for an alkyl group (or any substituent group not under scrutiny)
Ph	a phenyl group, the name of a benzene ring as a substituent, represented:



or



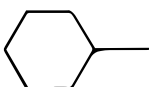
Ar	the general name for an aromatic group
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Symbols and Abbreviations, continued

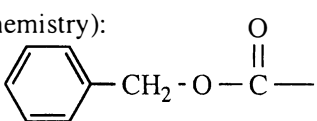
SUBSTITUENT GROUPS, continued

Ac an acetyl group: $\text{CH}_3-\overset{\text{O}}{\parallel}{\text{C}}-$

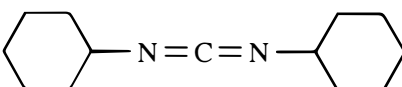
Cy a cyclohexyl group: 

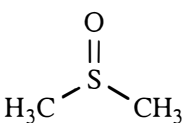
Ts tosyl, or *p*-toluenesulfonyl group: $\text{CH}_3-\text{C}_6\text{H}_4-\overset{\text{O}}{\parallel}{\text{S}}(\text{O})-$

Boc a *t*-butoxycarbonyl group (amino acid and peptide chemistry): $(\text{CH}_3)_3\text{C}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-$

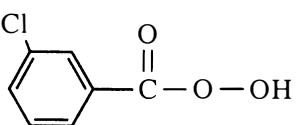
Z, or Cbz a carbobenzoxy (benzyloxycarbonyl) group (amino acid and peptide chemistry): 

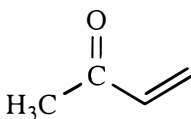
REAGENTS AND SOLVENTS

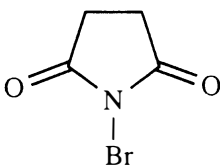
DCC dicyclohexylcarbodiimide 

DMSO dimethylsulfoxide 

ether diethyl ether, $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$

MCPBA *meta*-chloroperoxybenzoic acid 

MVK methyl vinyl ketone 

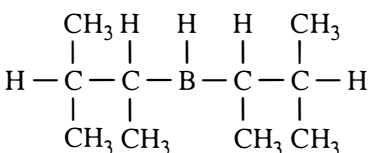
NBS *N*-bromosuccinimide 

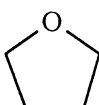
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Symbols and Abbreviations, continued

REAGENTS AND SOLVENTS, continued

PCC pyridinium chlorochromate, $\text{CrO}_3 \cdot \text{HCl} \cdot \text{N}$ 

Sia_2BH disiamylborane 

THF tetrahydrofuran 

SPECTROSCOPY

IR infrared spectroscopy
NMR nuclear **m**agnetic **r**esonance spectroscopy
MS **m**ass spectrometry
UV ultraviolet spectroscopy
ppm **p**arts **p**er **m**illion, a unit used in NMR
Hz hertz, cycles per second, a unit of frequency
MHz megahertz, millions of cycles per second
TMS tetra**m**ethylsilane, $(\text{CH}_3)_4\text{Si}$, the reference compound in NMR
s, d, t, q singlet, **d**oublet, **t**riplet, **q**uartet, referring to the number of peaks an NMR absorption gives
nm nanometers, 10^{-9} meters (usually used as a unit of wavelength)
m/z mass-to-charge ratio, in mass spectrometry
 δ in NMR, chemical shift value, measured in ppm
 λ wavelength
 ν frequency

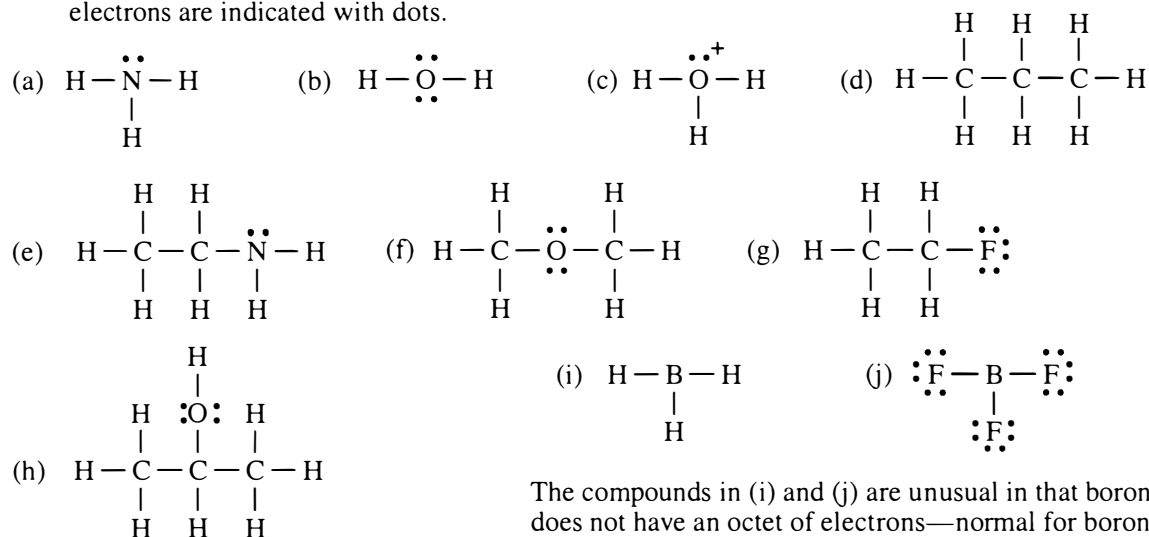
OTHER

a, *ax* axial (in chair forms of cyclohexane)
e, *eq* equatorial (in chair forms of cyclohexane)
HOMO highest **o**ccupied **m**olecular **o**rbital
LUMO lowest **u**noccupied **m**olecular **o**rbital
NR no reaction
o, *m*, *p* *ortho*, *meta*, *para* (positions on an aromatic ring)
 Δ when written over an arrow: "heat"; when written before a letter: "change in"
 δ^+ , δ^- partial positive charge, partial negative charge
 $h\nu$ energy from electromagnetic radiation (light)
 $[\alpha]_D$ specific rotation at the D line of sodium (589 nm)

CHAPTER 1—INTRODUCTION AND REVIEW

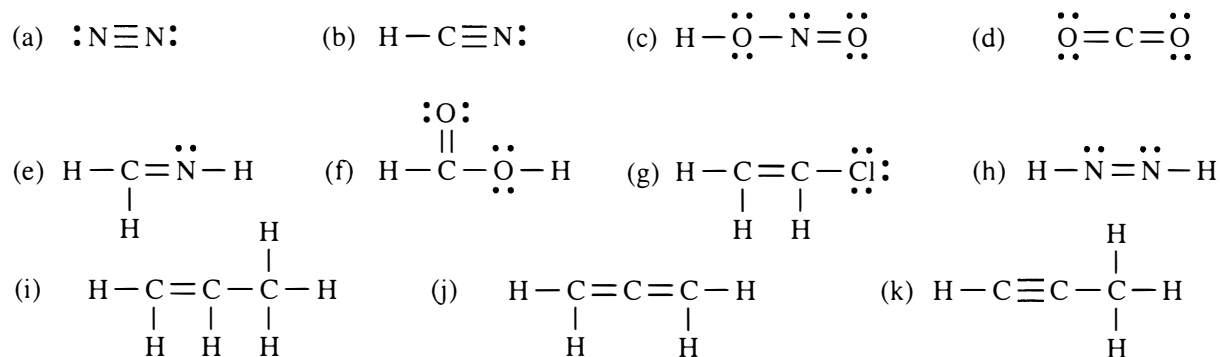
1-1	Na	$1s^2 2s^2 2p^6 3s^1$	P	$1s^2 2s^2 2p^6 3s^2 3p_x^1 3p_y^1 3p_z^1$
	Mg	$1s^2 2s^2 2p^6 3s^2$	S	$1s^2 2s^2 2p^6 3s^2 3p_x^2 3p_y^1 3p_z^1$
	Al	$1s^2 2s^2 2p^6 3s^2 3p_x^1$	Cl	$1s^2 2s^2 2p^6 3s^2 3p_x^2 3p_y^2 3p_z^1$
	Si	$1s^2 2s^2 2p^6 3s^2 3p_x^1 3p_y^1$	Ar	$1s^2 2s^2 2p^6 3s^2 3p_x^2 3p_y^2 3p_z^2$

1-2 In this book, lines between atom symbols represent covalent bonds between those atoms. Nonbonding electrons are indicated with dots.

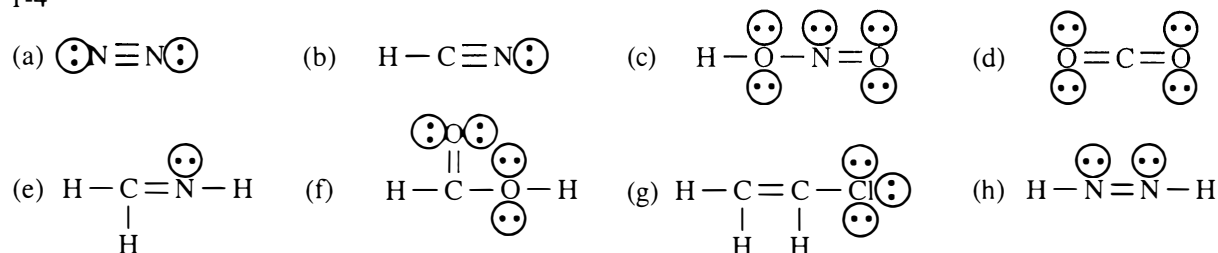


The compounds in (i) and (j) are unusual in that boron does not have an octet of electrons—normal for boron because it has only three valence electrons.

1-3

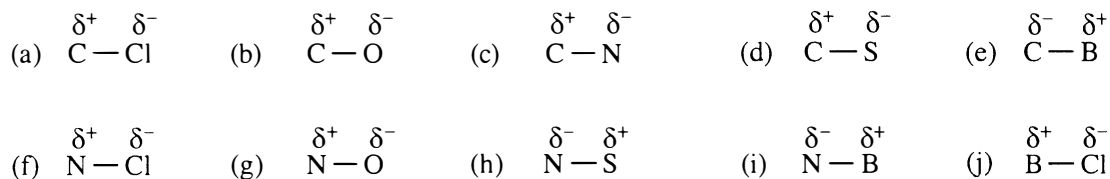


1-4

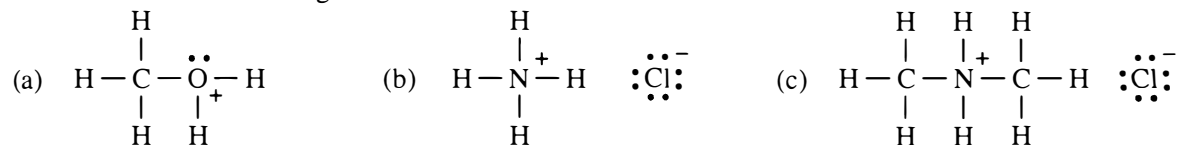


There are no unshared electron pairs in parts (i), (j), and (k).

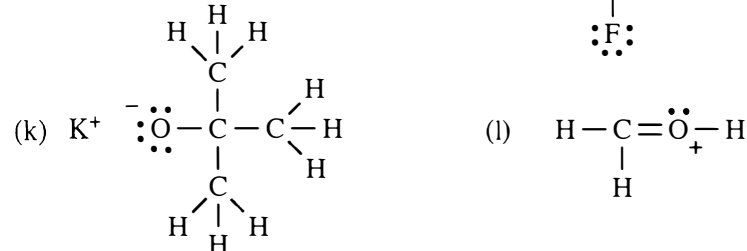
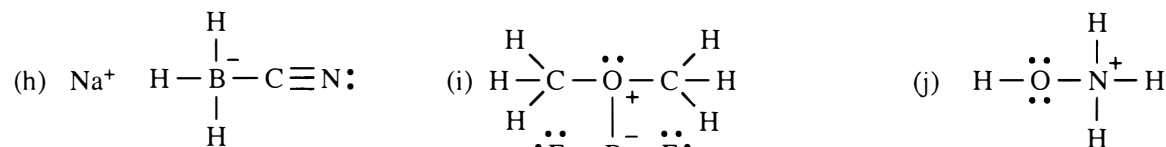
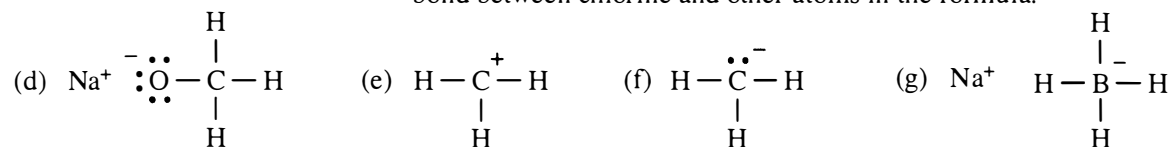
1-5 The symbols " δ^+ " and " δ^- " indicate bond polarity by showing partial charge. (In the arrow symbolism, the arrow should point to the partial negative charge.)



1-6 Non-zero formal charges are shown beside the atoms.

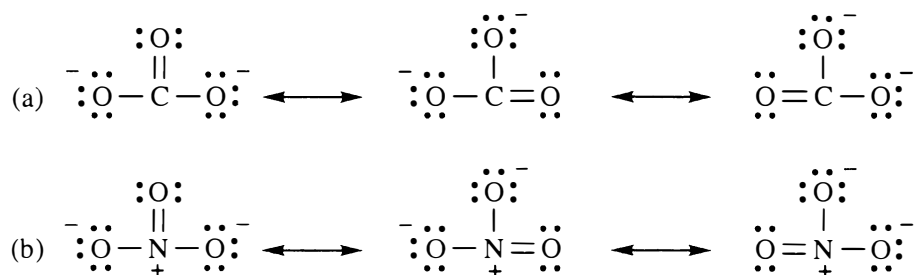


In (b) and (c), the chlorine is present as chloride ion. There is no covalent bond between chlorine and other atoms in the formula.

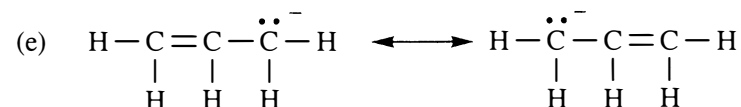
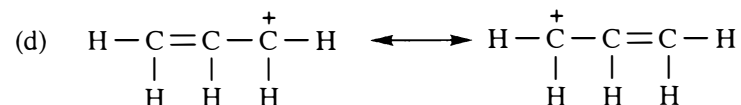
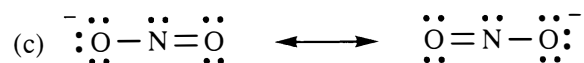


As shown in (d), (g), (h), and (k), alkali metals like sodium and potassium form only ionic bonds, never covalent bonds.

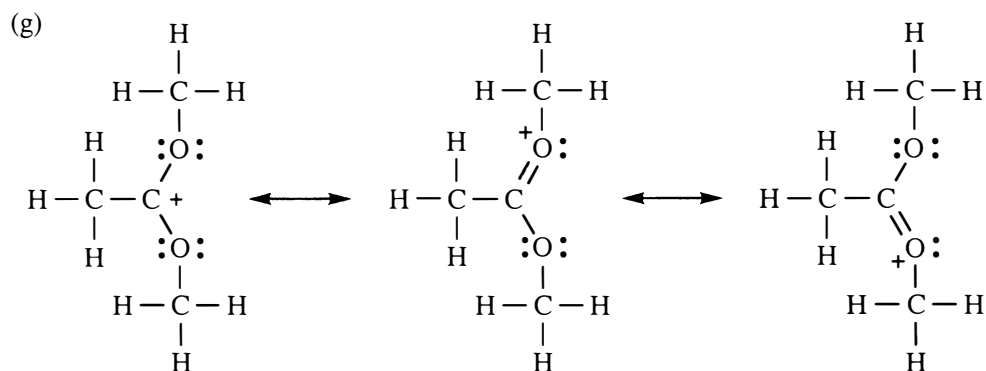
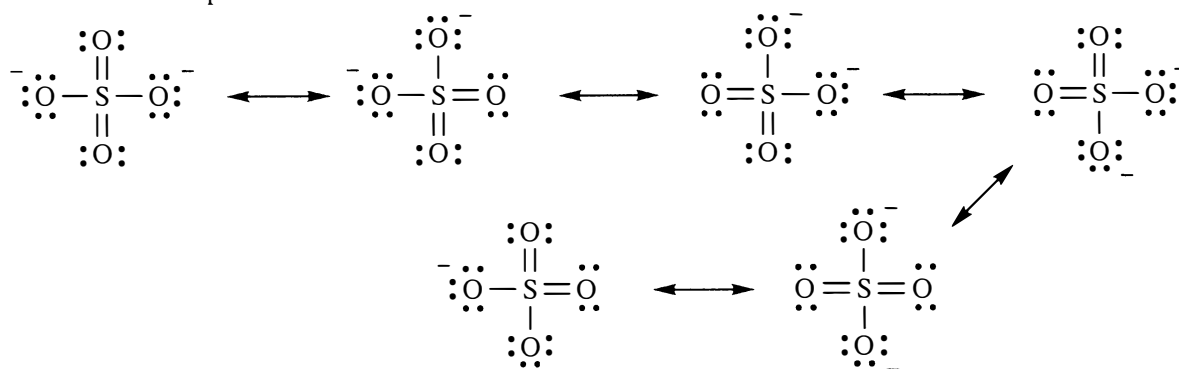
1-7 Resonance forms in which all atoms have full octets are the most significant contributors. In resonance forms, ALL ATOMS KEEP THEIR POSITIONS—ONLY ELECTRONS ARE SHOWN IN DIFFERENT POSITIONS.



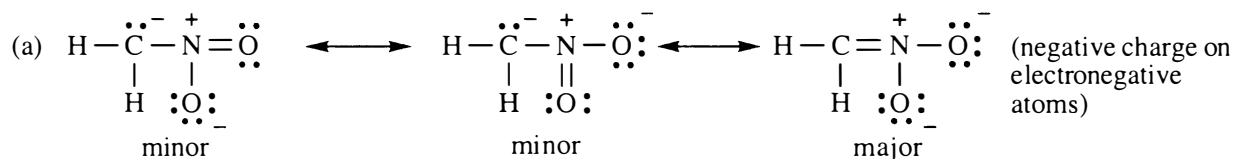
1-7 continued



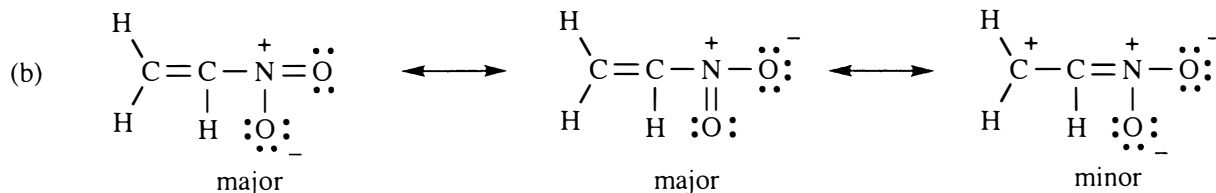
(f) Sulfur can have up to 12 electrons around it because it has d orbitals accessible.



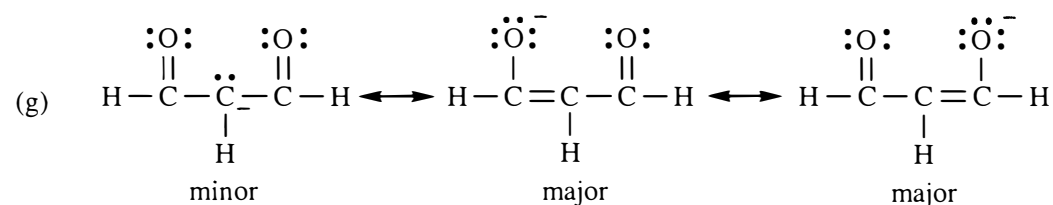
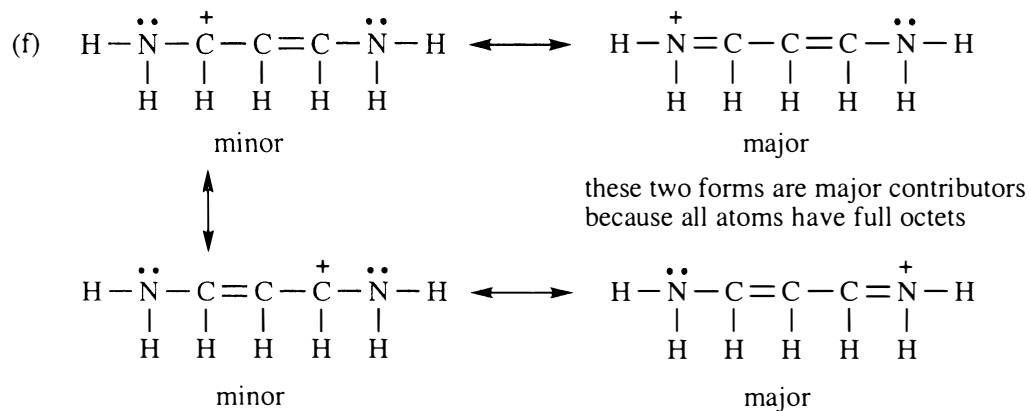
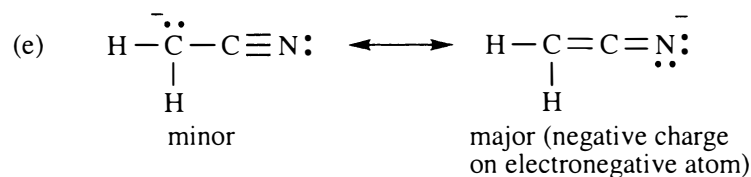
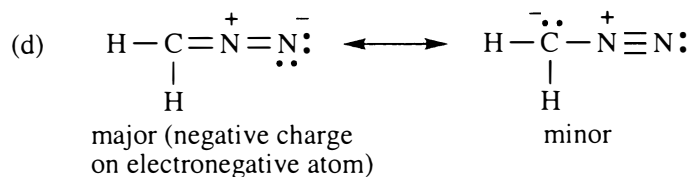
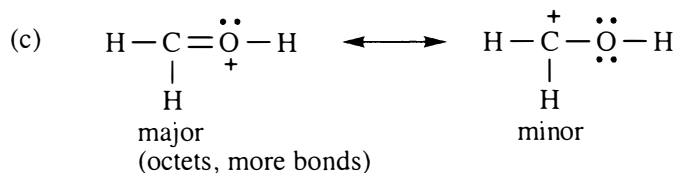
1-8 Major resonance contributors would have the lowest energy. The most important factors are: maximize full octets; maximize bonds; put negative charge on electronegative atoms; minimize charge separation.



1-8 continued

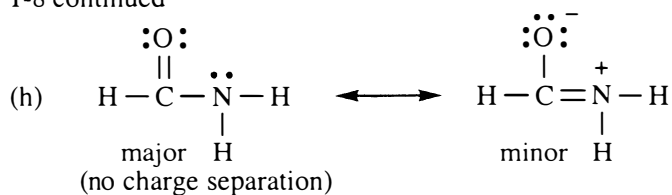


These two forms have equivalent energy and are major because they have full octets, more bonds, and less charge separation than the minor contributor.

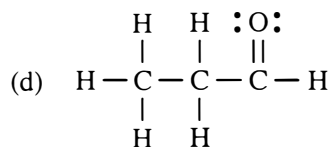
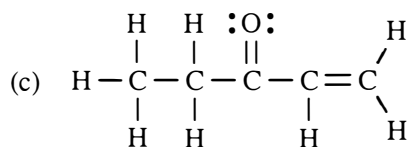
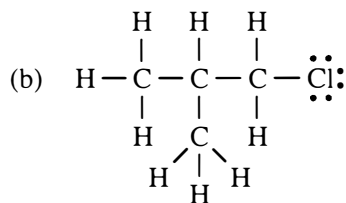
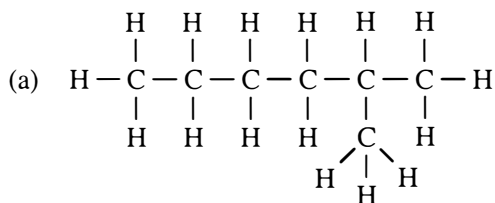


these two have equivalent energy and are major because the negative charge is on the more electronegative oxygen atom

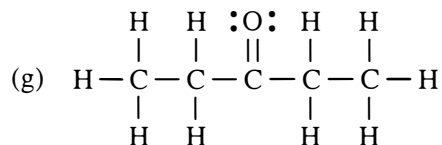
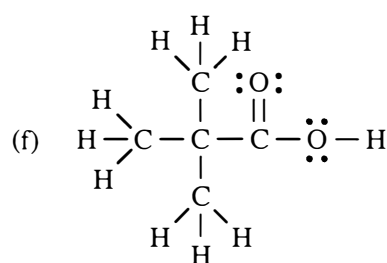
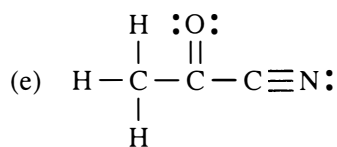
1-8 continued



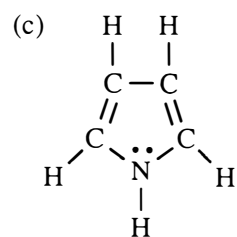
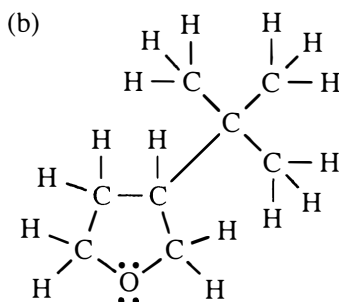
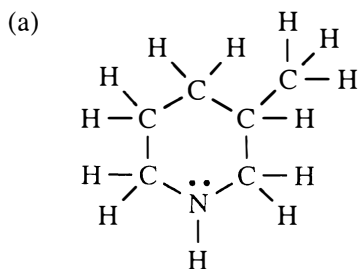
1-9 Your Lewis structures may *appear* different from these. As long as the atoms are connected in the same order and by the same type of bond, they are equivalent structures. For now, the exact placement of the atoms on the page is not significant. A Lewis structure is "complete" with unshared electron pairs shown.



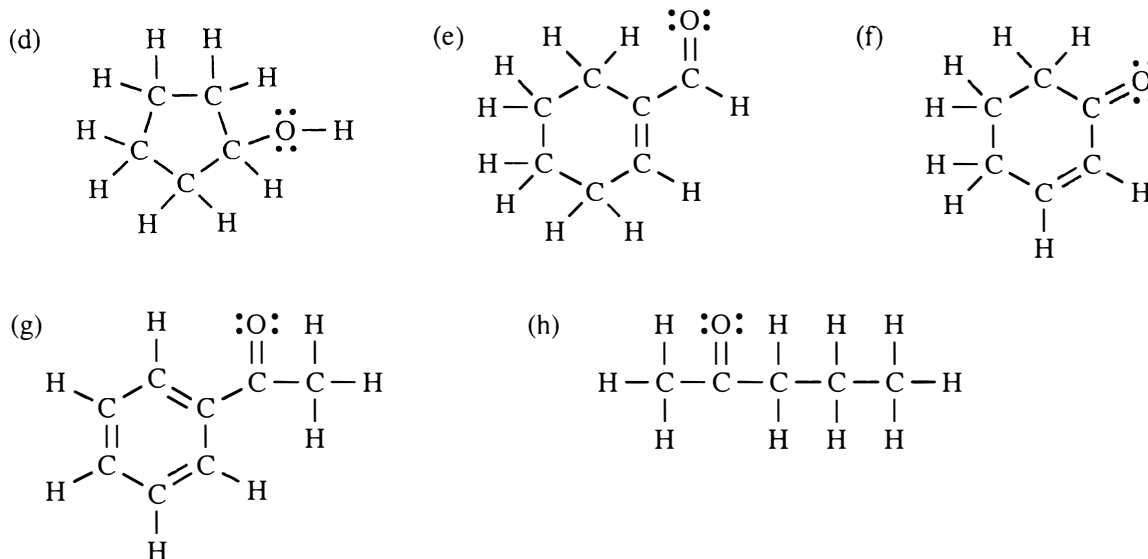
Always be alert for the implied double or triple bond. Remember that C has to have four bonds, nitrogen has three bonds, oxygen has two bonds, and hydrogen has one bond. The only exceptions to these valence rules are structures with formal charges.



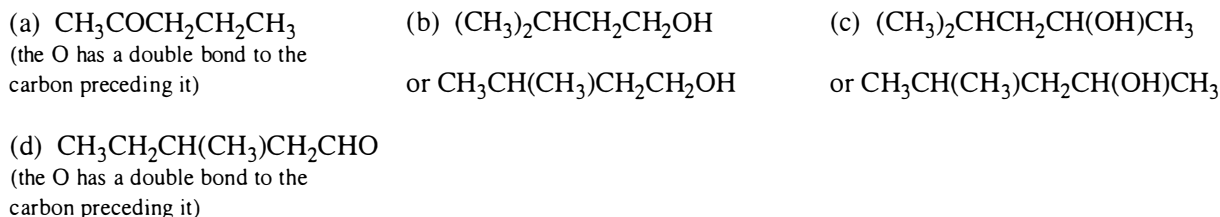
1-10 Complete Lewis structures show all atoms, bonds, and unshared electron pairs.



1-10 continued



1-11 There is often more than one correct way to write condensed structural formulas. You must often make inferences about what a condensed formula means according to valence rules, especially in structures with C=O as shown in parts (a) and (d).



1-12 If the percent values do not sum to 100%, the remainder must be oxygen. Assume 100 g of sample; percents then translate directly to grams of each element.

There are usually many possible structures for a molecular formula. Yours may be different from the examples shown here.

(a) $\frac{40.0 \text{ g C}}{12.0 \text{ g/mole}} = 3.33 \text{ moles C} \div 3.33 \text{ moles} = 1 \text{ C}$

$\frac{6.67 \text{ g H}}{1.01 \text{ g/mole}} = 6.60 \text{ moles H} \div 3.33 \text{ moles} = 1.98 \approx 2 \text{ H}$

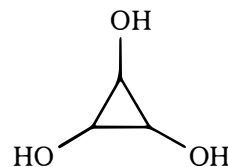
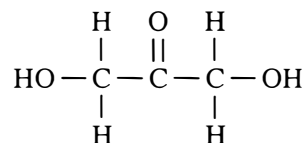
$\frac{53.33 \text{ g O}}{16.0 \text{ g/mole}} = 3.33 \text{ moles O} \div 3.33 \text{ moles} = 1 \text{ O}$

empirical formula = $\boxed{\text{CH}_2\text{O}}$ $\Rightarrow$ empirical weight = 30

molecular weight = 90, three times the empirical weight $\Rightarrow$

three times the empirical formula = molecular formula = $\boxed{\text{C}_3\text{H}_6\text{O}_3}$

some possible structures:



MANY other structures possible.

1-12 continued

$$(b) \frac{32.0 \text{ g C}}{12.0 \text{ g/mole}} = 2.67 \text{ moles C} \div 1.34 \text{ moles} = 1.99 \approx 2 \text{ C}$$

$$\frac{6.67 \text{ g H}}{1.01 \text{ g/mole}} = 6.60 \text{ moles H} \div 1.34 \text{ moles} = 4.93 \approx 5 \text{ H}$$

$$\frac{18.7 \text{ g N}}{14.0 \text{ g/mole}} = 1.34 \text{ moles N} \div 1.34 \text{ moles} = 1 \text{ N}$$

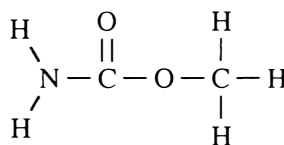
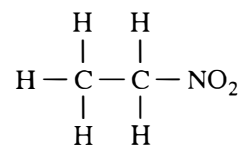
$$\frac{42.6 \text{ g O}}{16.0 \text{ g/mole}} = 2.66 \text{ moles O} \div 1.34 \text{ moles} = 1.99 \approx 2 \text{ O}$$

empirical formula = $\boxed{\text{C}_2\text{H}_5\text{NO}_2}$ $\Rightarrow$ empirical weight = 75

molecular weight = 75, same as the empirical weight $\Rightarrow$

empirical formula = molecular formula = $\boxed{\text{C}_2\text{H}_5\text{NO}_2}$

some possible structures:



MANY other structures possible.

$$(c) \frac{37.2 \text{ g C}}{12.0 \text{ g/mole}} = 3.10 \text{ moles C} \div 1.55 \text{ moles} = 2 \text{ C}$$

$$\frac{7.75 \text{ g H}}{1.01 \text{ g/mole}} = 7.67 \text{ moles H} \div 1.55 \text{ moles} = 4.95 \approx 5 \text{ H}$$

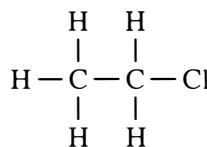
$$\frac{55.0 \text{ g Cl}}{35.45 \text{ g/mole}} = 1.55 \text{ moles Cl} \div 1.55 \text{ moles} = 1 \text{ Cl}$$

empirical formula = $\boxed{\text{C}_2\text{H}_5\text{Cl}}$ $\Rightarrow$ empirical weight = 64.46

molecular weight = 64, same as the empirical weight $\Rightarrow$

empirical formula = molecular formula = $\boxed{\text{C}_2\text{H}_5\text{Cl}}$

There is only one structure possible with this molecular formula:



$$(d) \frac{38.4 \text{ g C}}{12.0 \text{ g/mole}} = 3.20 \text{ moles C} \div 1.60 \text{ moles} = 2 \text{ C}$$

$$\frac{4.80 \text{ g H}}{1.01 \text{ g/mole}} = 4.75 \text{ moles H} \div 1.60 \text{ moles} = 2.97 \approx 3 \text{ H}$$

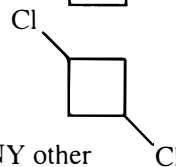
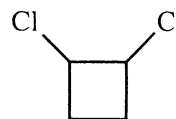
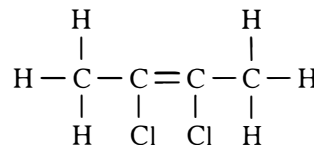
$$\frac{56.8 \text{ g Cl}}{35.45 \text{ g/mole}} = 1.60 \text{ moles Cl} \div 1.60 \text{ moles} = 1 \text{ Cl}$$

empirical formula = $\boxed{\text{C}_2\text{H}_3\text{Cl}}$ $\Rightarrow$ empirical weight = 62.45

molecular weight = 125, twice the empirical weight $\Rightarrow$

twice the empirical formula = molecular formula = $\boxed{\text{C}_4\text{H}_6\text{Cl}_2}$

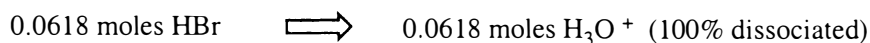
some possible structures:



MANY other structures possible.

1-13

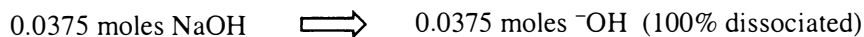
$$(a) \quad 5.00 \text{ g HBr} \times \frac{1 \text{ mole HBr}}{80.9 \text{ g HBr}} = 0.0618 \text{ moles HBr}$$



$$\frac{0.0618 \text{ moles H}_3\text{O}^+}{100 \text{ mL}} \times \frac{1000 \text{ mL}}{1 \text{ L}} = \frac{0.618 \text{ moles H}_3\text{O}^+}{1 \text{ L solution}}$$

$$\text{pH} = -\log_{10} [\text{H}_3\text{O}^+] = -\log_{10} (0.618) = \boxed{0.209}$$

$$(b) \quad 1.50 \text{ g NaOH} \times \frac{1 \text{ mole NaOH}}{40.0 \text{ g NaOH}} = 0.0375 \text{ moles NaOH}$$



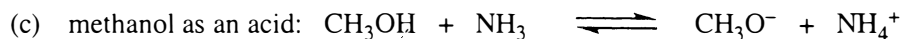
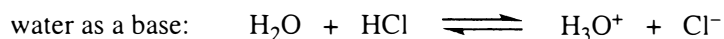
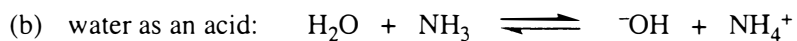
$$\frac{0.0375 \text{ moles } ^-\text{OH}}{50. \text{ mL}} \times \frac{1000 \text{ mL}}{1 \text{ L}} = \frac{0.75 \text{ moles } ^-\text{OH}}{1 \text{ L solution}} = 0.75 \text{ M}$$

$$[\text{H}_3\text{O}^+] = \frac{1 \times 10^{-14}}{[\text{ } ^-\text{OH}]} = \frac{1 \times 10^{-14}}{0.75} = 1.33 \times 10^{-14}$$

$$\text{pH} = -\log_{10} [\text{H}_3\text{O}^+] = -\log_{10} (1.33 \times 10^{-14}) = \boxed{13.88} \quad \text{(the number of decimal places in a pH value is the number of significant figures)}$$

1-14

(a) By definition, an acid is any species that can donate a proton. Ammonia has a proton bonded to nitrogen, so ammonia can be an acid (although a very weak one). A base is a proton acceptor, that is, it must have a pair of electrons to share with a proton; in theory, any atom with an unshared electron pair can be a base. The nitrogen in ammonia has an unshared electron pair so ammonia is basic. In water, ammonia is too weak an acid to give up its proton; instead, it acts as a base and pulls a proton from water to a small extent.



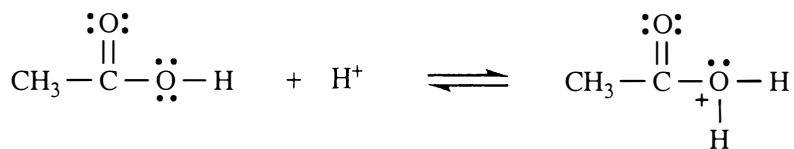
1-15

- (a) $\text{HCOOH} + \text{CN}^- \rightleftharpoons \text{HCOO}^- + \text{HCN}$
 stronger acid pK_a 3.76 + stronger base weaker base weaker acid pK_a 9.22 **FAVORS PRODUCTS**
- (b) $\text{CH}_3\text{COO}^- + \text{CH}_3\text{OH} \rightleftharpoons \text{CH}_3\text{COOH} + \text{CH}_3\text{O}^-$
 weaker base weaker acid pK_a 15.5 stronger acid pK_a 4.74 stronger base **FAVORS REACTANTS**
- (c) $\text{CH}_3\text{OH} + \text{NaNH}_2 \rightleftharpoons \text{CH}_3\text{O}^- \text{Na}^+ + \text{NH}_3$
 stronger acid pK_a 15.5 stronger base weaker base weaker acid pK_a 33 **FAVORS PRODUCTS**
- (d) $\text{Na}^+ \text{OCH}_3^- + \text{HCN} \rightleftharpoons \text{HOCH}_3 + \text{NaCN}$
 stronger base stronger acid pK_a 9.22 weaker acid pK_a 15.5 weaker base **FAVORS PRODUCTS**
- (e) $\text{HCl} + \text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{Cl}^-$
 stronger acid stronger base weaker acid weaker base **FAVORS PRODUCTS**
- (f) $\text{H}_3\text{O}^+ + \text{CH}_3\text{O}^- \rightleftharpoons \text{H}_2\text{O} + \text{CH}_3\text{OH}$
 stronger acid pK_a -1.7 stronger base weaker base weaker acid pK_a 15.5 **FAVORS PRODUCTS**

The first reaction in Table 1-5 shows the K_{eq} for this reaction is 160, favoring products.

The seventh reaction in Table 1-5 shows the K_{eq} for the *reverse* of this reaction is 3.2×10^{-16} . Therefore, K_{eq} for this reaction as written must be the inverse, or 3.1×10^{15} , strongly favoring products.

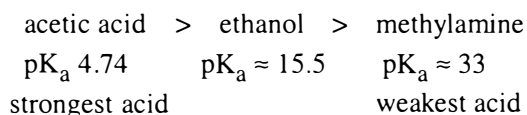
1-16



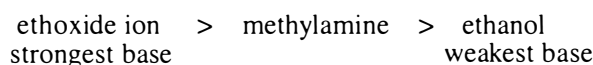
Protonation of the double-bonded oxygen gives three resonance forms (as shown in Solved Problem 1-5(c)); protonation of the single-bonded oxygen gives only one. In general, the more resonance forms a species has, the more stable it is, so the proton would bond to the oxygen that gives a more stable species, that is, the double-bonded oxygen.

1-17 In Solved Problem 1-4, the structures of ethanol and methylamine are shown to be similar to methanol and ammonia, respectively. We must infer that their acid-base properties are also similar.

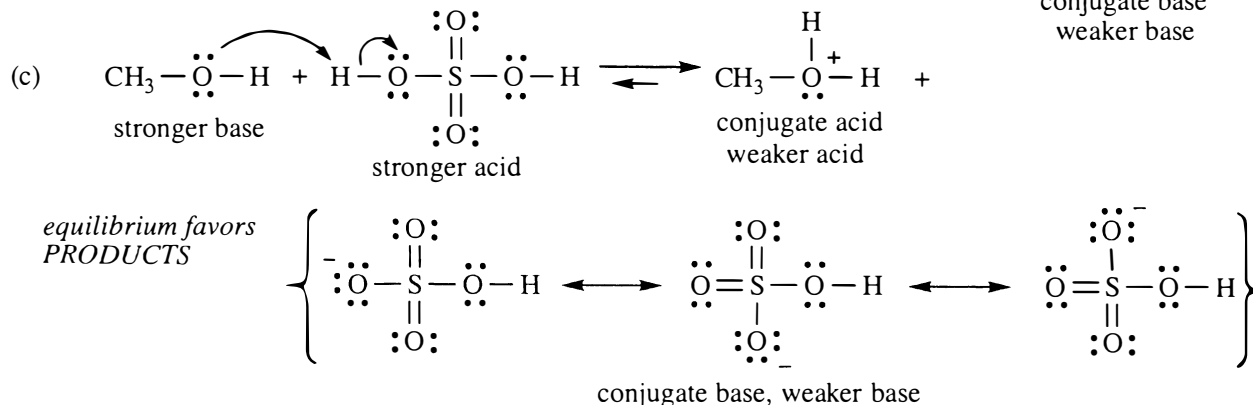
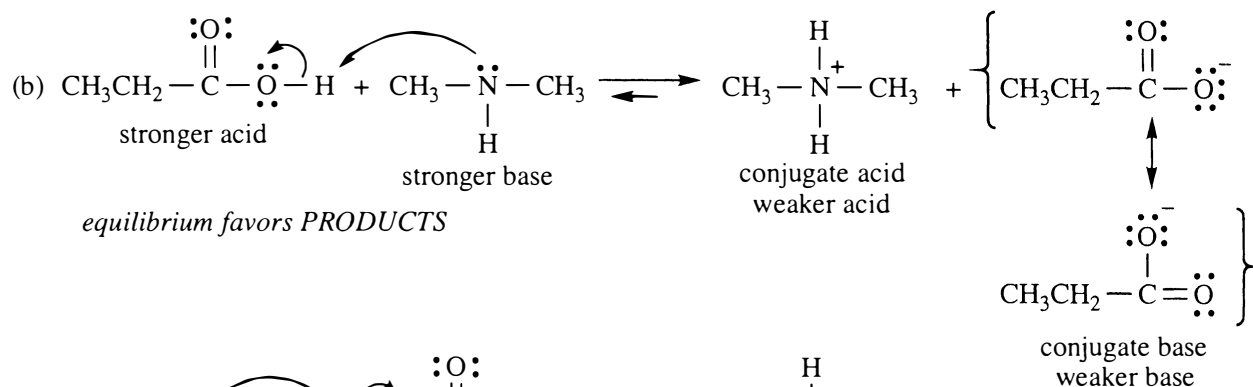
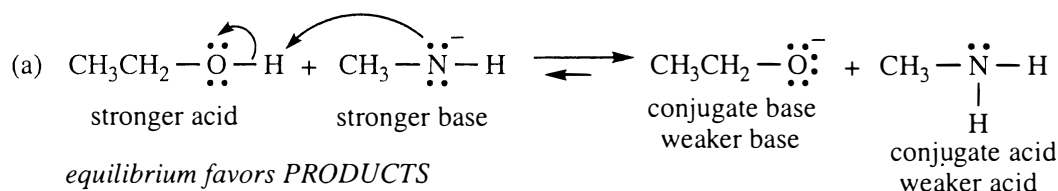
(a) This problem can be viewed in two ways. 1) Quantitatively, the pK_a values determine the order of acidity. 2) Qualitatively, the stabilities of the conjugate bases determine the order of acidity (see Solved Problem 1-4 for structures): the conjugate base of acetic acid, acetate ion, is resonance-stabilized, so acetic acid is the most acidic; the conjugate base of ethanol has a negative charge on a very electronegative oxygen atom; the conjugate base of methylamine has a negative charge on a mildly electronegative nitrogen atom and is therefore the least stabilized, so methylamine is the least acidic.



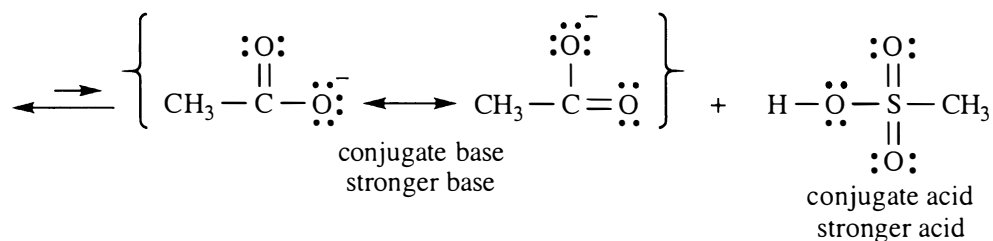
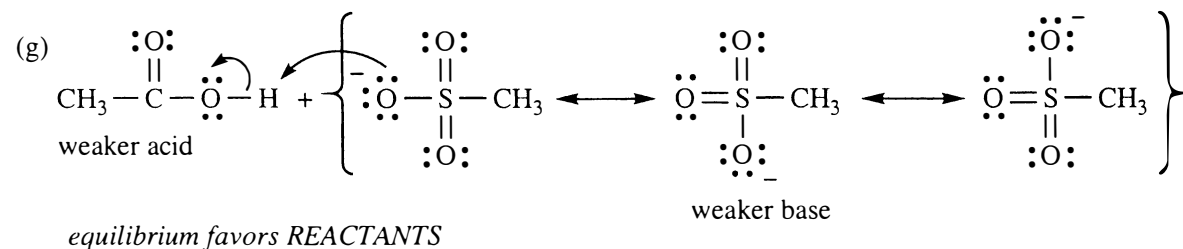
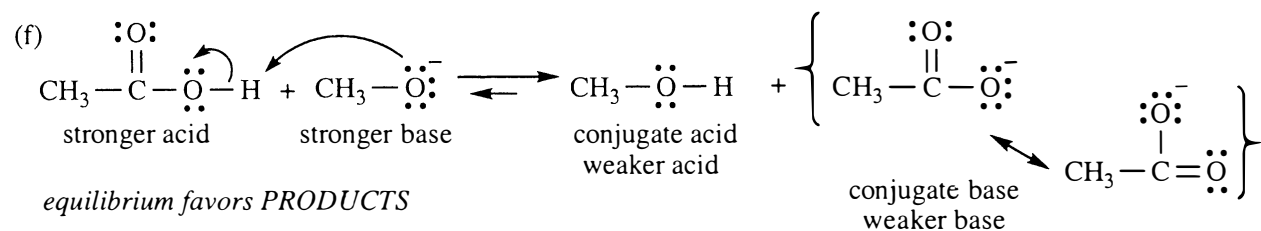
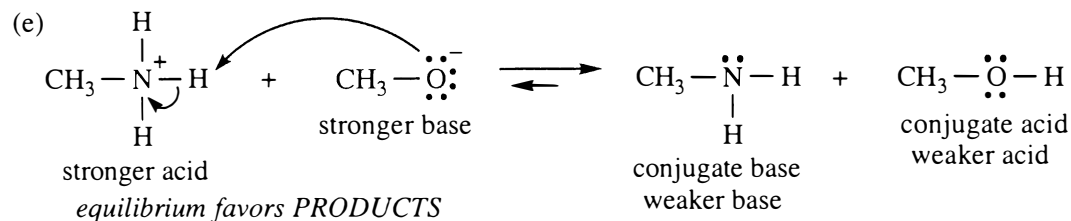
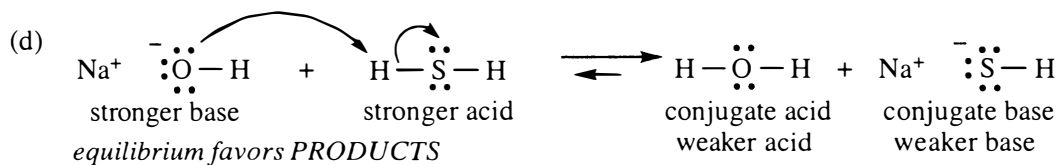
(b) Ethoxide ion is the conjugate base of ethanol, so it must be a stronger base than ethanol; Solved Problem 1-4 indicates ethoxide is analogous to hydroxide in base strength. Methylamine has pK_b 3.36. The basicity of methylamine is between the basicity of ethoxide ion and ethanol.



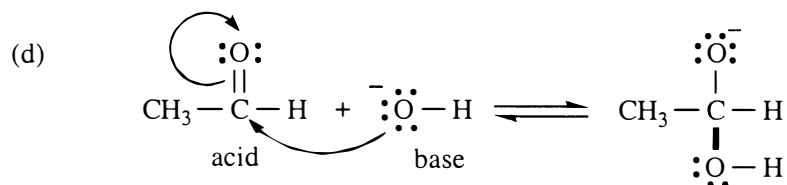
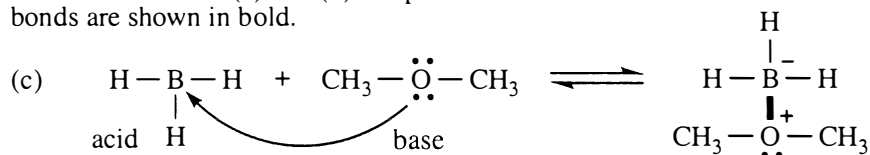
1-18 Curved arrows show electron movement, as described in text section 1-14.



1-18 continued

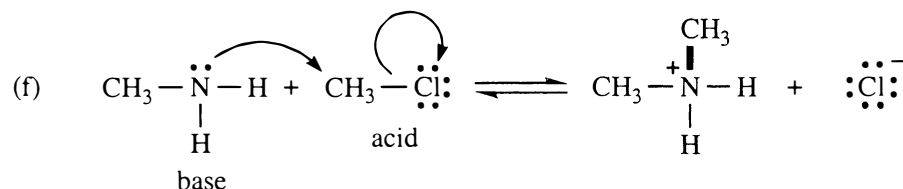
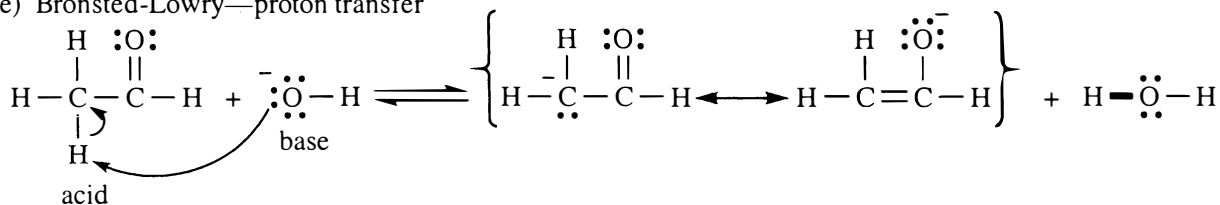


1-19 Solutions for (a) and (b) are presented in the Solved Problem in the text. Here, the newly formed bonds are shown in bold.



1-19 continued

(e) Bronsted-Lowry—proton transfer



1-20

Learning organic chemistry is similar to learning a foreign language: new vocabulary, new grammar (the reactions), some new concepts, and even a new alphabet (the symbolism of chemistry). This type of definition question is intended to help you review the vocabulary and concepts in each chapter. All of the definitions and examples are presented in the Glossary and in the chapter, so this Solutions Manual will not repeat them. Use these questions to evaluate your comprehension and to guide your review of the important concepts in the chapter.

1-21 (a) CARBON! (b) oxygen (c) phosphorus (d) chlorine

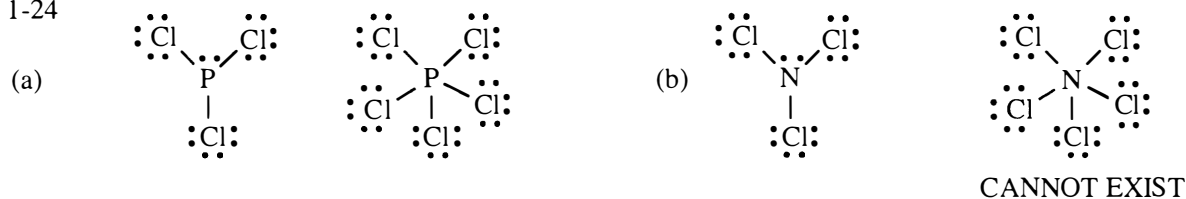
1-22

valence e ⁻ →	1	2	3	4	5	6	7	8
	H							He (2e ⁻)
	Li	Be	B	C	N	O	F	Ne
					P	S	Cl	
							Br	
							I	

1-23

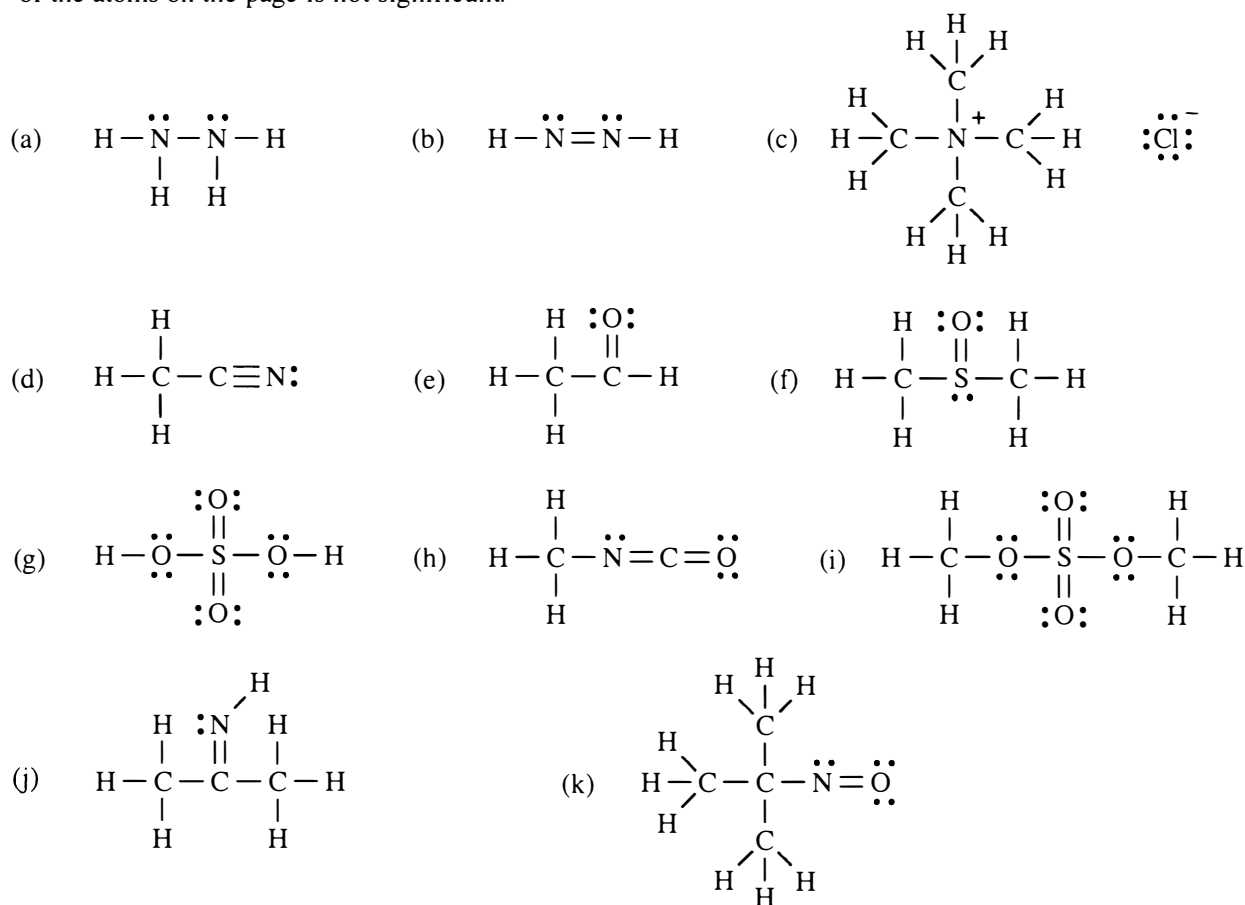
- (a) ionic only (b) covalent (H—O⁻) and ionic (Na⁺ ⁻OH)
- (c) covalent (H—C and C—Li), but the C—Li bond is strongly polarized
- (d) covalent only (e) covalent (H—C and C—O⁻) and ionic (Na⁺ ⁻OCH₃)
- (f) covalent (H—C and C=O and C—O⁻) and ionic (HCO₂⁻ Na⁺) (g) covalent only

1-24

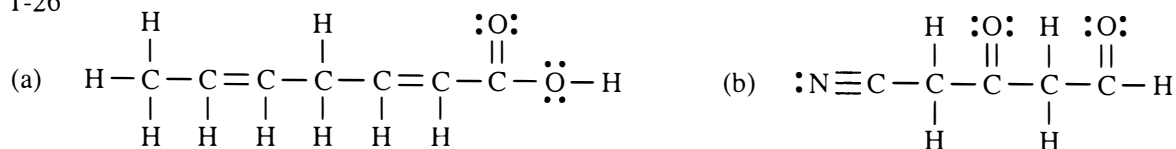


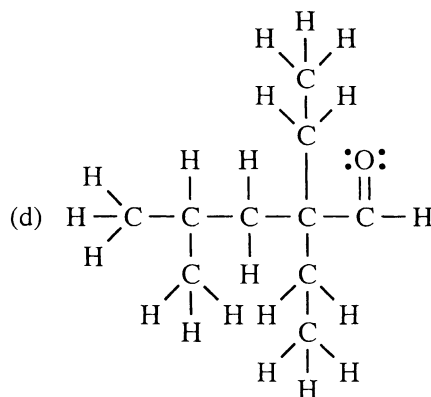
NCl_5 violates the octet rule; nitrogen can have no more than eight electrons (or four atoms) around it. Phosphorus, a third-row element, can have more than eight electrons because phosphorus can use orbitals in bonding, so PCl_5 is a stable, isolable compound.

1-25 Your Lewis structures may look different from these. As long as the atoms are connected in the same order and by the same type of bond, they are equivalent structures. For now, the exact placement of the atoms on the page is not significant.

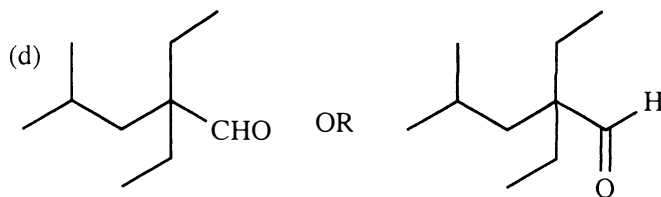
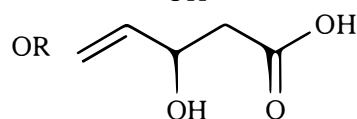
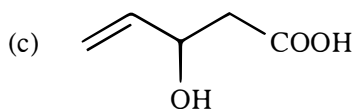
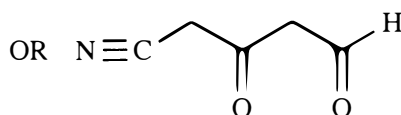
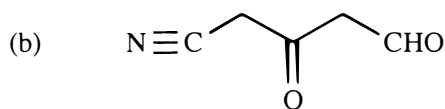
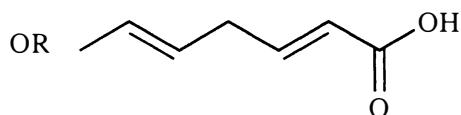


1-26



$$\begin{array}{ccccccc} & & \text{H} & \cdot\cdot & \text{H} & \text{:O:} & \\ & & | & & | & || & \\ \text{(c)} & \text{H}-\text{C}=\text{C}-\text{C}-\text{C}-\text{C}-\ddot{\text{O}}-\text{H} \\ & | & | & | & | & & \\ & \text{H} & \text{H} & \text{H} & \text{H} & & \end{array}$$


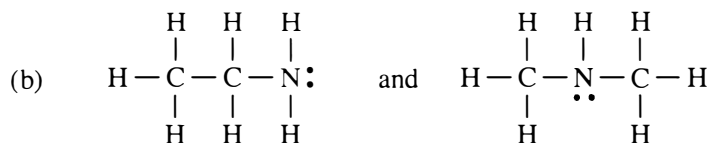
(a) 



1-28

(a)
$$\begin{array}{ccccccc} & \text{H} & \text{H} & \text{H} & \text{H} & & \\ & | & | & | & | & & \\ \text{H} & -\text{C} & -\text{C} & -\text{C} & -\text{C} & -\text{H} & \\ & | & | & | & | & & \\ & \text{H} & \text{H} & \text{H} & \text{H} & & \end{array} \quad \text{and} \quad \begin{array}{ccccccc} & \text{H} & \text{H} & \text{H} & & & \\ & | & | & | & & & \\ \text{H} & -\text{C} & -\text{C} & -\text{C} & -\text{H} & & \\ & | & & | & & & \\ & \text{H} & & \text{C} & & \text{H} & \\ & & \text{H} & | & \text{H} & & \\ & & & \text{H} & & & \end{array}$$

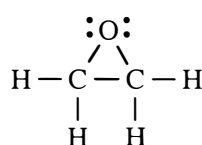
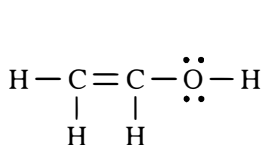
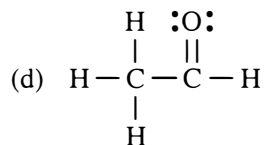
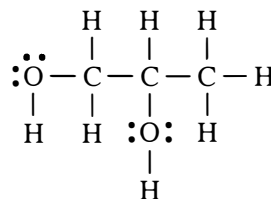
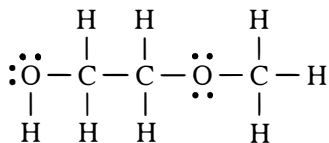
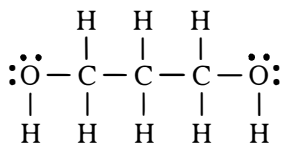
these are the only two possibilities, but your structures may appear different—making models will help you visualize these structures



these are the only two possibilities, but your structures may appear different—making models will help you visualize these structures

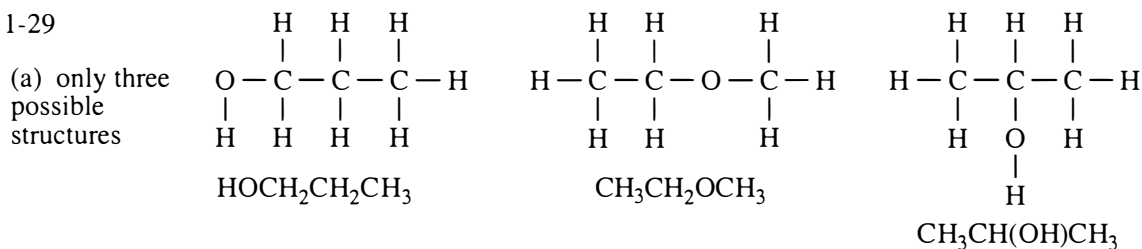
1-28 continued

(c) There are several other possibilities as well. Your answer may be correct even if it does not appear here. Check with others in your study group.

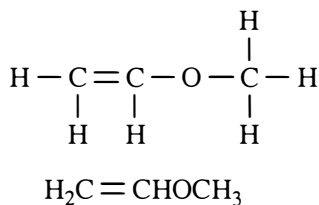
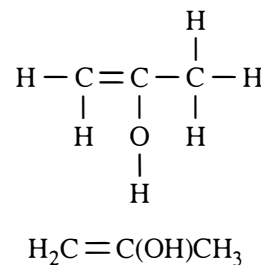
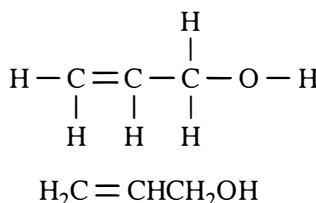
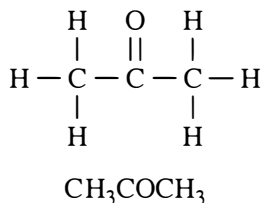
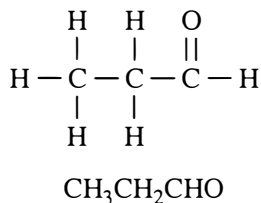


These are the only three structures with this molecular formula.

1-29

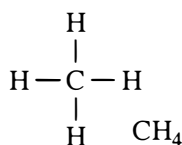


(b) There are several other possibilities as well.

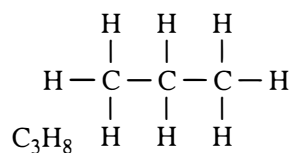
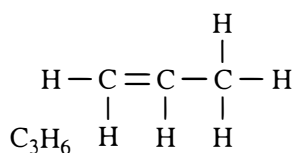
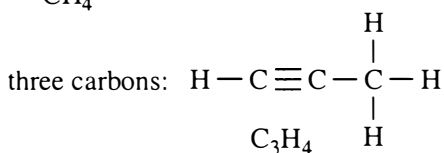
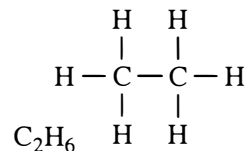
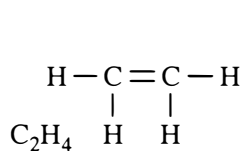
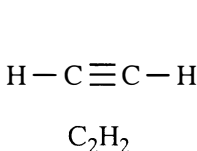


1-30 General rule: *molecular formulas of stable hydrocarbons must have an even number of hydrogens.* The formula CH_2 does not have enough atoms to bond with the four orbitals of carbon.

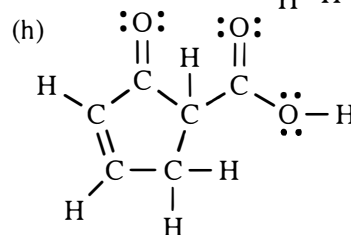
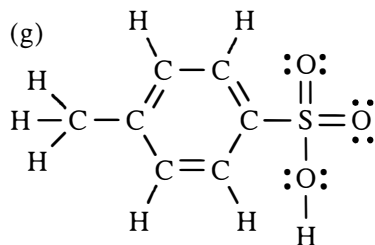
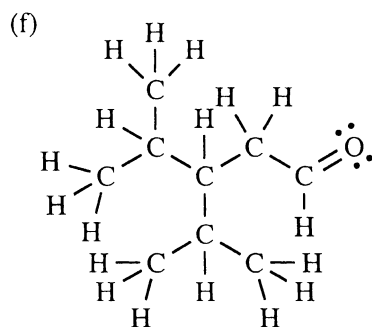
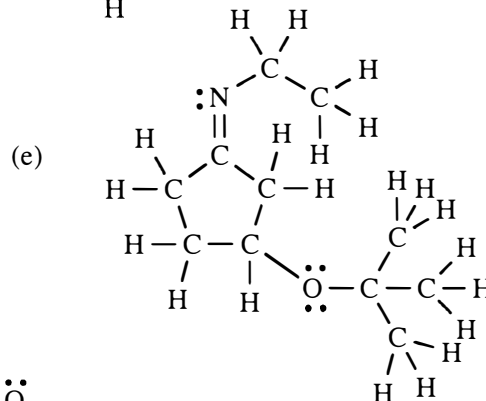
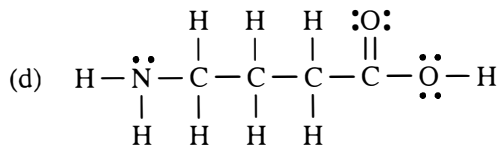
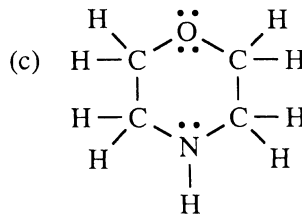
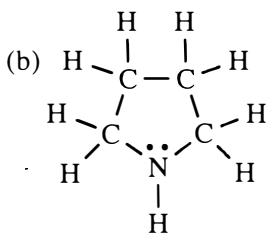
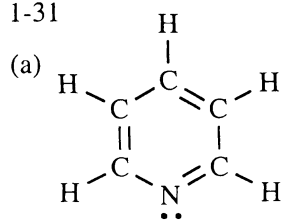
one carbon:



two carbons:



1-31

1-32 (a) C_5H_5N (b) C_4H_9N (c) C_4H_9NO (d) $C_4H_9NO_2$ (e) $C_{11}H_{21}NO$ (f) $C_9H_{18}O$ (g) $C_7H_8O_3S$ (h) $C_6H_6O_3$

1-33

(a) $100\% - 62.0\% C - 10.4\% H = 27.6\% \text{ oxygen}$

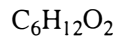
$$\frac{62.0 \text{ g C}}{12.0 \text{ g/mole}} = 5.17 \text{ moles C} \div 1.73 \text{ moles} = 2.99 \approx 3 \text{ C}$$

$$\frac{10.4 \text{ g H}}{1.01 \text{ g/mole}} = 10.3 \text{ moles H} \div 1.73 \text{ moles} = 5.95 \approx 6 \text{ H}$$

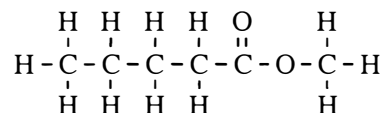
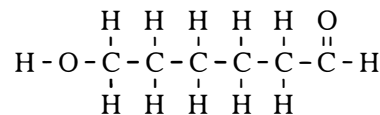
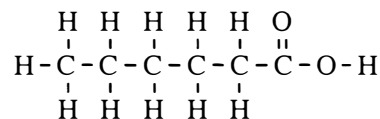
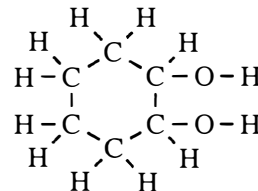
$$\frac{27.6 \text{ g O}}{16.0 \text{ g/mole}} = 1.73 \text{ moles O} \div 1.73 \text{ moles} = 1 \text{ O}$$

(b) empirical formula = C_3H_6O $\Rightarrow$ empirical weight = 58

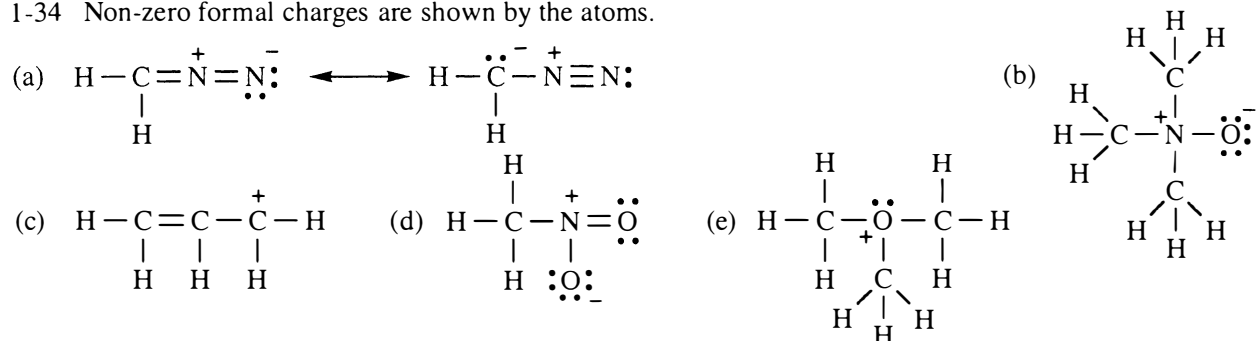
molecular weight = 117, about double the empirical weight

 $\Rightarrow$ double the empirical formula = molecular formula =

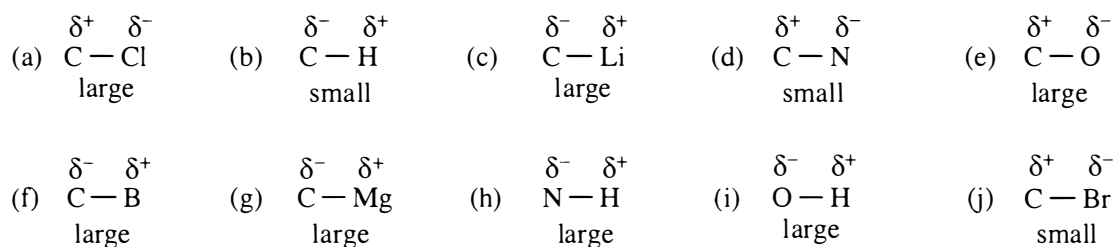
(c) some possible structures—MANY other structures possible:



1-34 Non-zero formal charges are shown by the atoms.



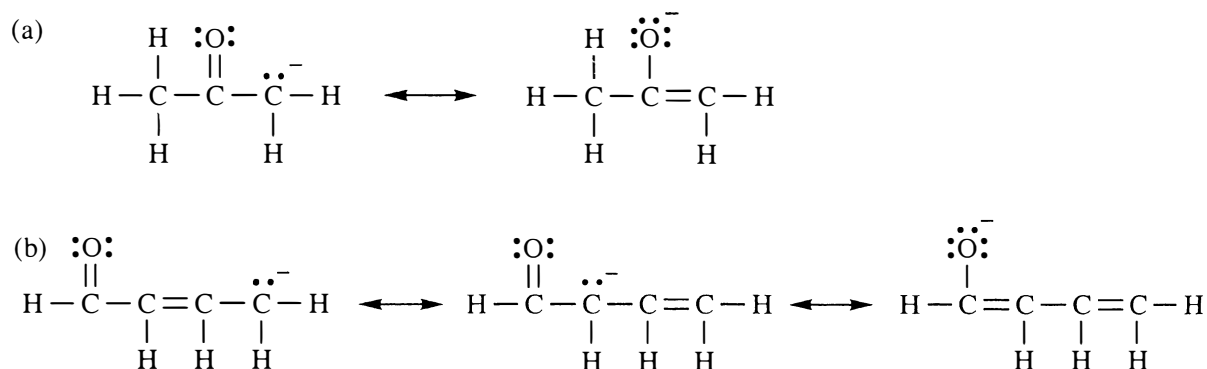
1-35 The symbols " δ^+ " and " δ^- " indicate bond polarity by showing partial charge. Electronegativity differences greater than or equal to 0.5 are considered large.



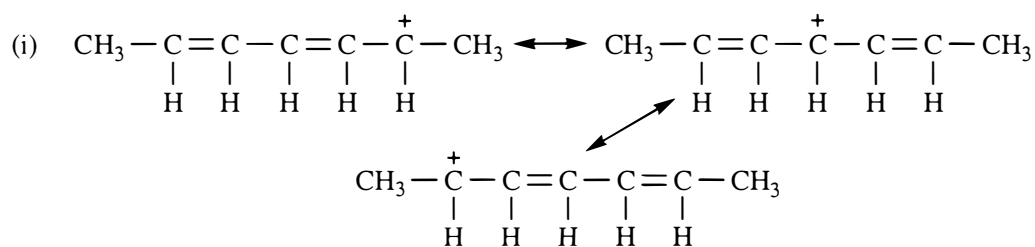
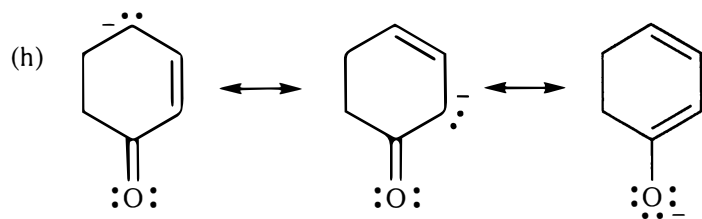
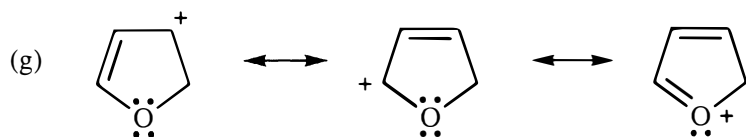
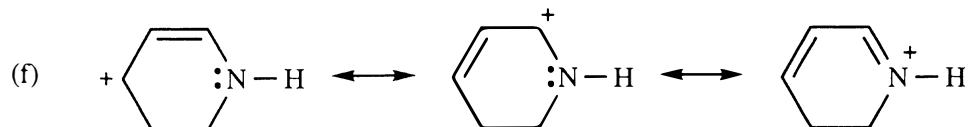
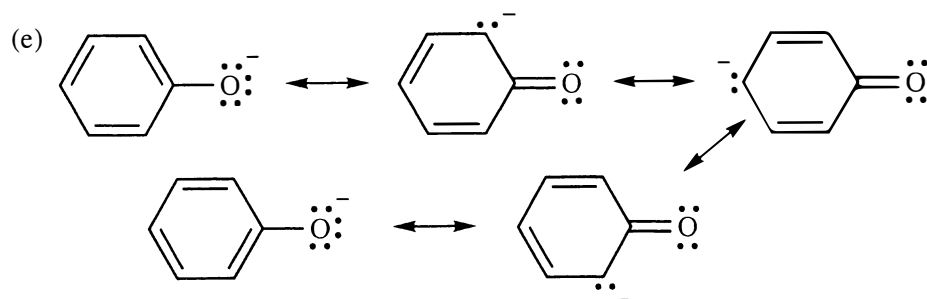
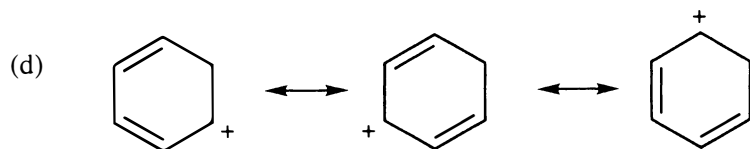
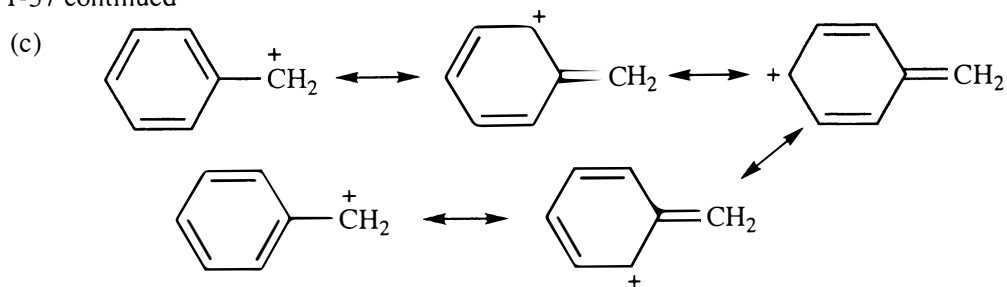
1-36 Resonance forms must have atoms in identical positions. If any atom moves position, it is a different structure.

- (a) different compounds—a hydrogen atom has changed position
 (b) resonance forms—only the position of electrons is different
 (c) resonance forms—only the position of electrons is different
 (d) resonance forms—only the position of electrons is different
 (e) different compounds—a hydrogen atom has changed position
 (f) resonance forms—only the position of electrons is different
 (g) resonance forms—only the position of electrons is different
 (h) different compounds—a hydrogen atom has changed position
 (i) resonance forms—only the position of electrons is different
 (j) resonance forms—only the position of electrons is different

1-37

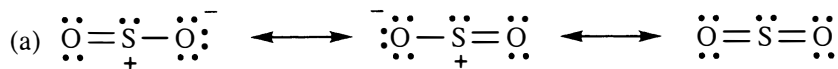


1-37 continued



(j) no resonance forms—the charge must be on an atom next to a double or triple bond, or next to a non-bonded pair of electrons, in order for resonance to delocalize the charge

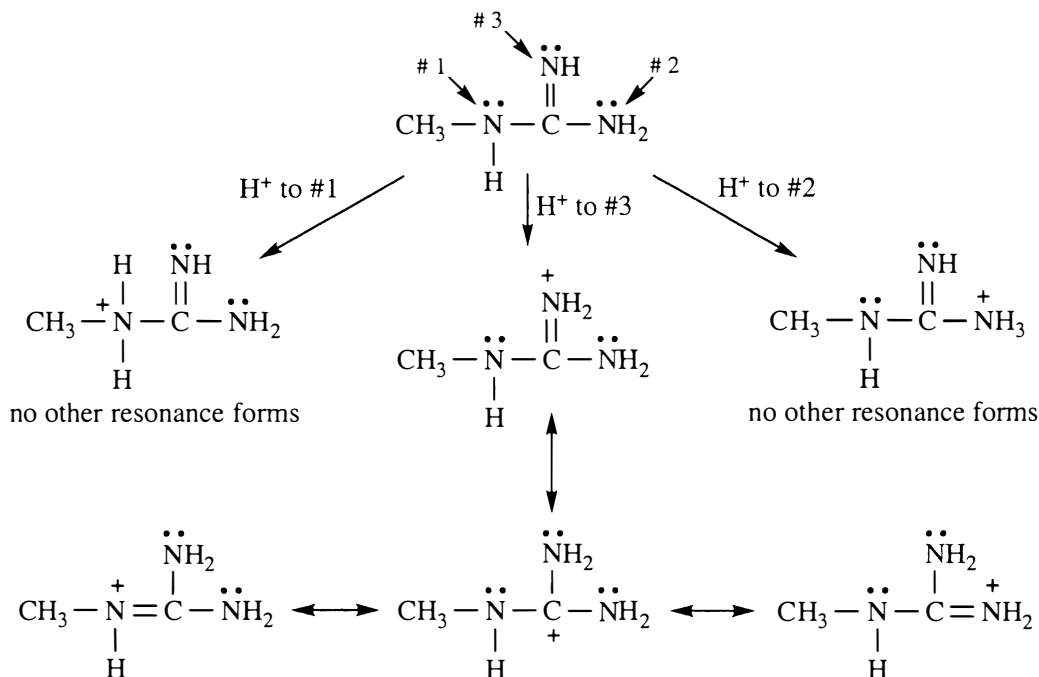
1-38



(c) The last resonance form of SO_2 has no equivalent form in O_3 . Sulfur, a third row element, can have more than eight electrons around it because of d orbitals, whereas oxygen, a second row element, must adhere strictly to the octet rule.

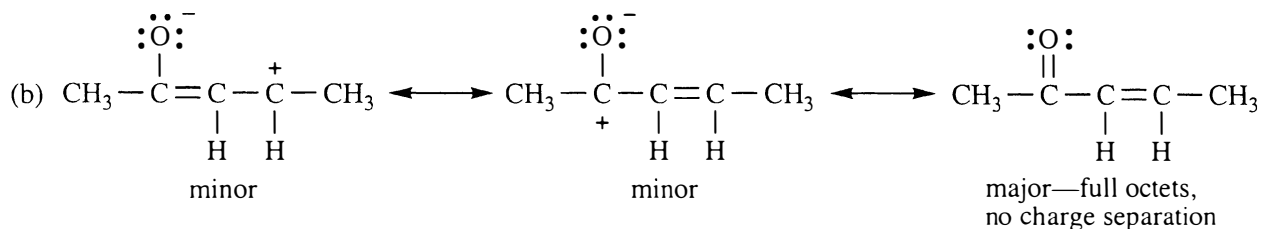
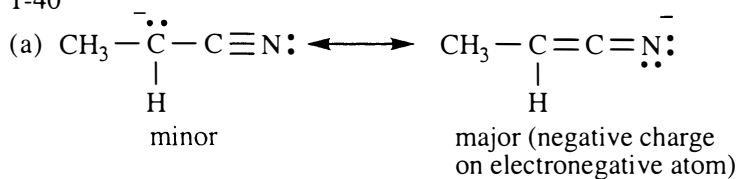
1-39

(a)

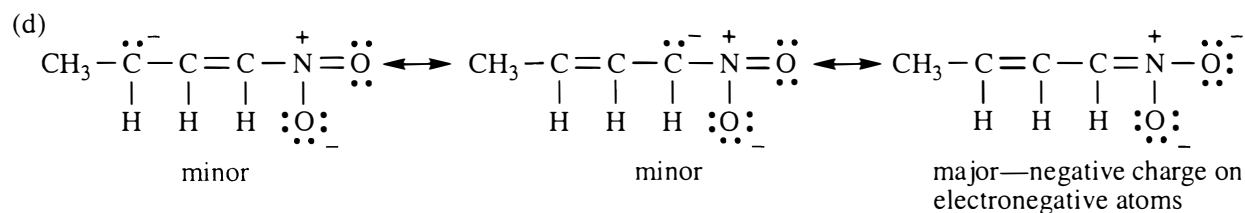
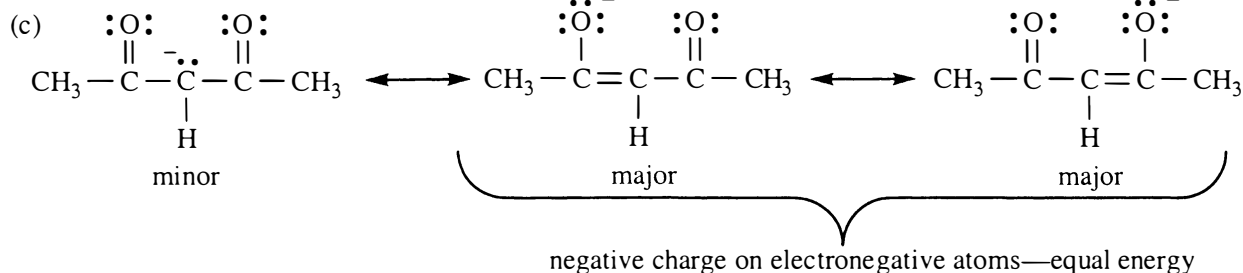


(b) Protonation at nitrogen #3 gives four resonance forms that delocalize the positive charge over all three nitrogens and a carbon—a very stable condition. Nitrogen #3 will be protonated preferentially, which we interpret as being more basic.

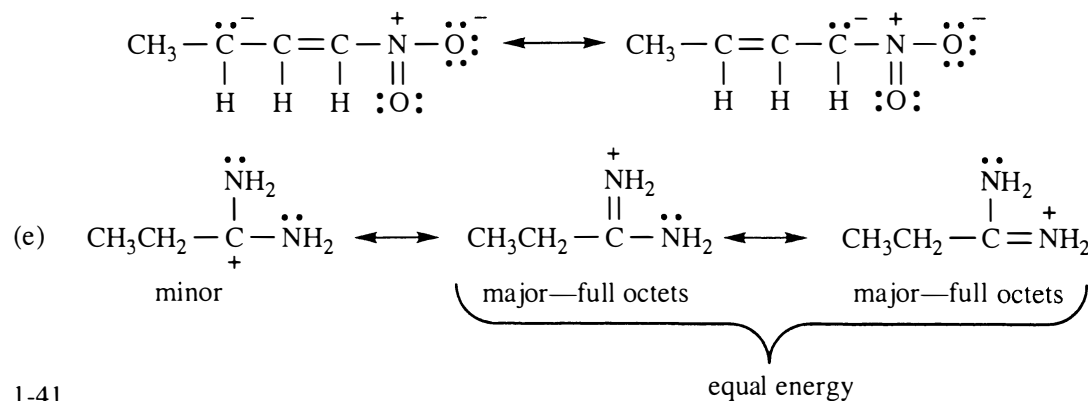
1-40



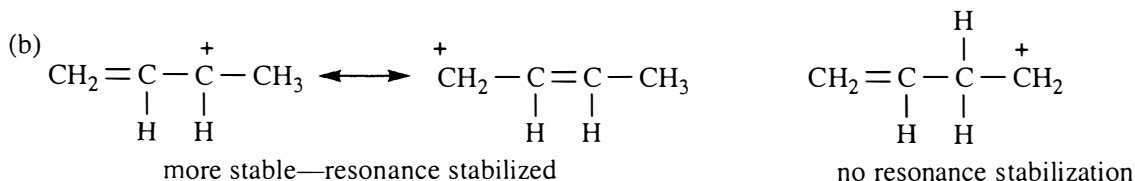
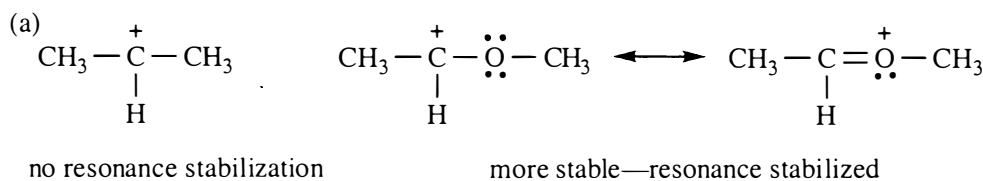
1-40 continued



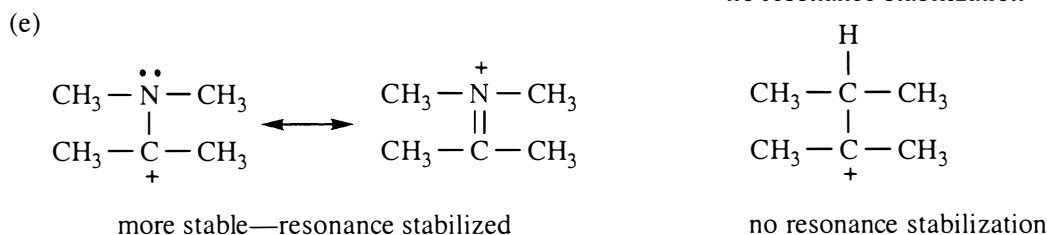
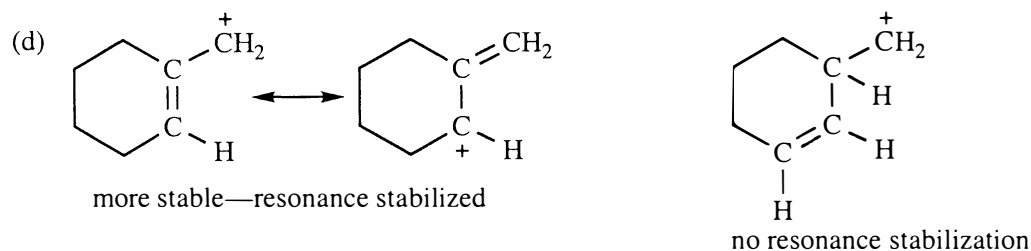
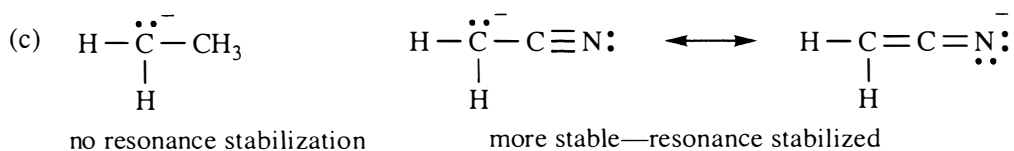
NOTE: The two structures below are resonance forms, varying from the first two structures in part (d) by the different positions of the double bonds in the NO_2 . Usually, chemists omit drawing the second form of the NO_2 group although we all understand that its presence is implied. It is good idea to draw all the resonance forms until they become second nature. The importance of understanding resonance forms cannot be overemphasized.



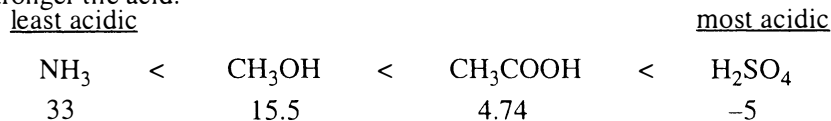
1-41



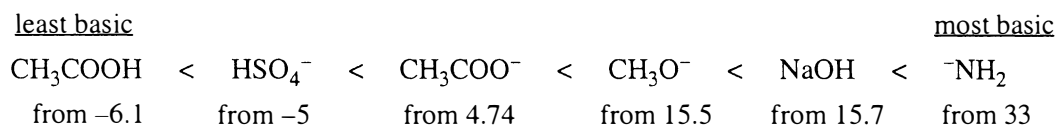
1-41 continued



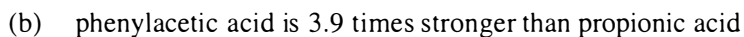
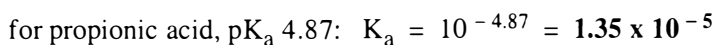
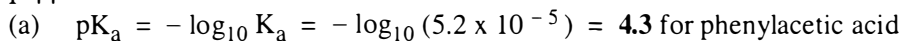
1-42 These pK_a values from the text, Table 1-5, and Appendix 5 provide the answers. The lower the pK_a , the stronger the acid.



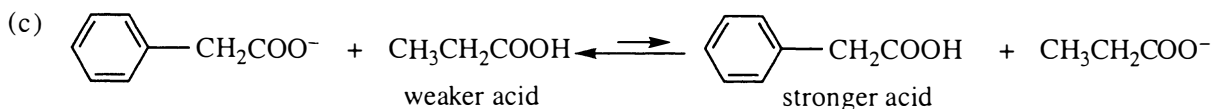
1-43 Conjugate bases of the weakest acids will be the strongest bases. The pK_a values of the conjugate acids are listed here. (The relative order of the first two was determined from the pK_a values of sulfuric acid and protonated acetic acid in Appendix 5 of the textbook.)



1-44

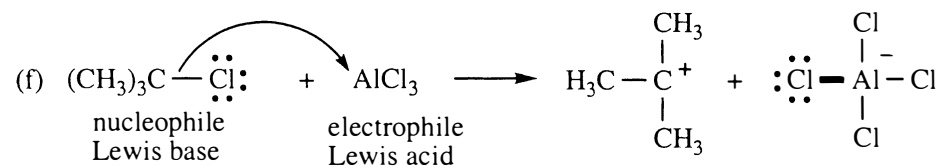
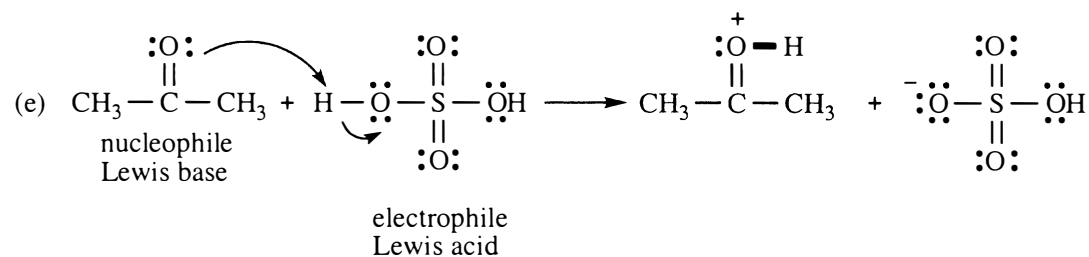
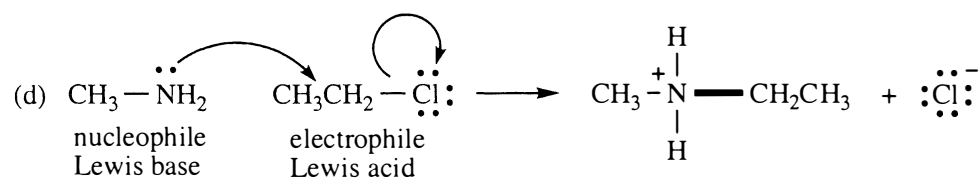
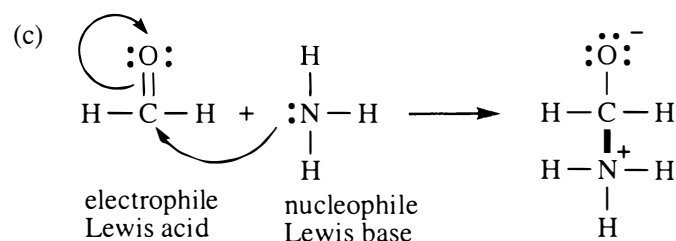
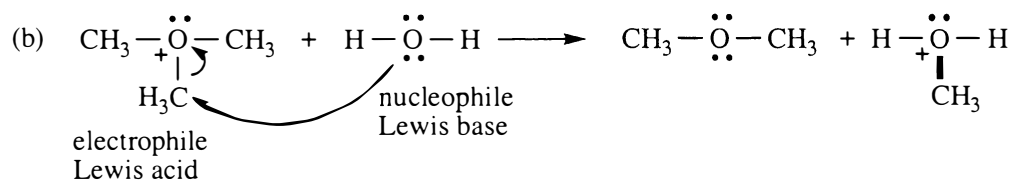
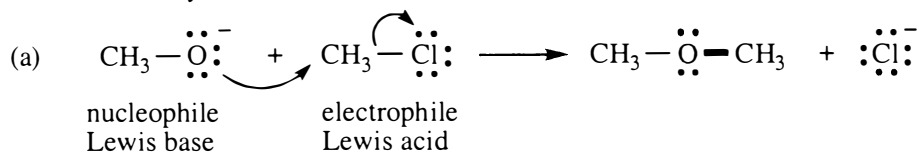


$$\frac{5.2 \times 10^{-5}}{1.35 \times 10^{-5}} = 3.9$$

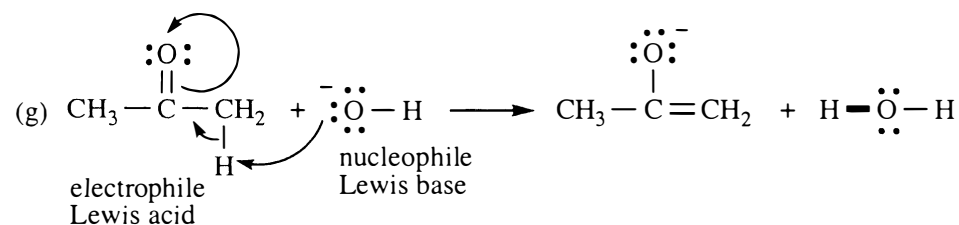


Equilibrium favors the weaker acid and base. In this reaction, **reactants** are favored.

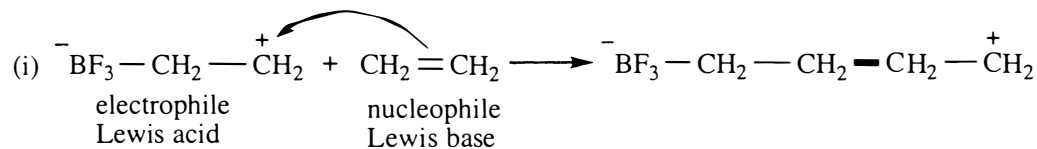
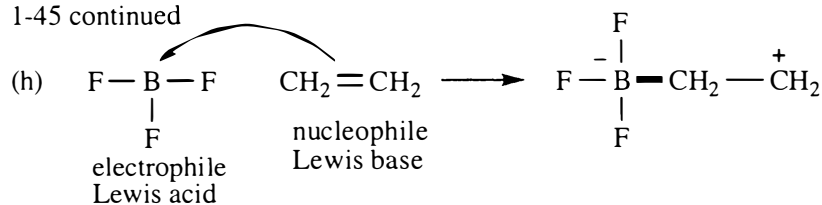
1-45 The newly formed bond is shown in bold.



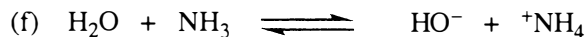
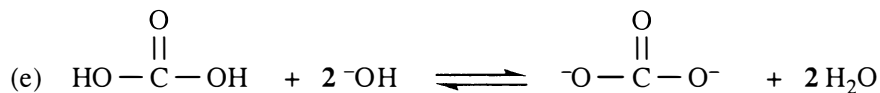
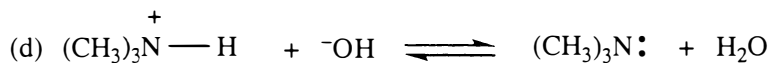
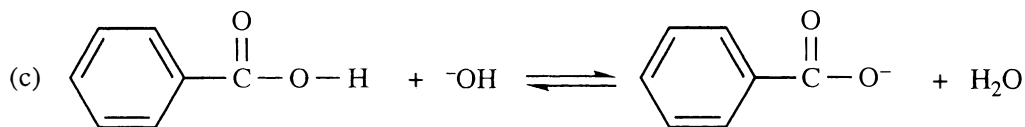
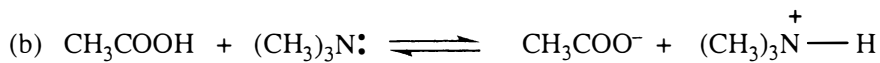
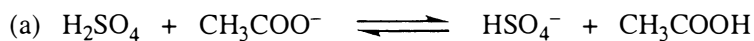
This may also be written in two steps: association of the Cl with Al, and a second step where the C—Cl bond breaks.



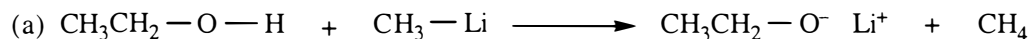
1-45 continued



1-46



1-47



(b) The conjugate acid of CH_3Li is CH_4 . Table 1-5 gives the pK_a of CH_4 as > 40 , one of the weakest acids known. The conjugate base of one of the weakest acids known must be one of the strongest bases known.

1-48

From the amounts of CO₂ and H₂O generated, the milligrams of C and H in the original sample can be determined, thus giving by difference the amount of oxygen in the 5.00 mg sample. From these values, the empirical formula and empirical weight can be calculated.

(a) how much carbon in 14.54 mg CO₂

$$14.54 \text{ mg CO}_2 \times \frac{1 \text{ mmole CO}_2}{44.01 \text{ mg CO}_2} \times \frac{1 \text{ mmole C}}{1 \text{ mmole CO}_2} \times \frac{12.01 \text{ mg C}}{1 \text{ mmole C}} = 3.968 \text{ mg C}$$

how much hydrogen in 3.97 mg H₂O

$$3.97 \text{ mg H}_2\text{O} \times \frac{1 \text{ mmole H}_2\text{O}}{18.016 \text{ mg H}_2\text{O}} \times \frac{2 \text{ mmoles H}}{1 \text{ mmole H}_2\text{O}} \times \frac{1.008 \text{ mg H}}{1 \text{ mmole H}} = 0.444 \text{ mg H}$$

how much oxygen in 5.00 mg estradiol

$$5.00 \text{ mg estradiol} - 3.968 \text{ mg C} - 0.444 \text{ mg H} = 0.59 \text{ mg O}$$

calculate empirical formula

$$\frac{3.968 \text{ mg C}}{12.01 \text{ mg/mole}} = 0.3304 \text{ mmoles C} \div 0.037 \text{ mmoles} = 8.93 \approx 9 \text{ C}$$

$$\frac{0.444 \text{ mg H}}{1.008 \text{ mg/mole}} = 0.440 \text{ mmoles H} \div 0.037 \text{ mmoles} = 11.9 \approx 12 \text{ H}$$

$$\frac{0.59 \text{ mg O}}{16.00 \text{ mg/mole}} = 0.037 \text{ mmoles O} \div 0.037 \text{ mmoles} = 1 \text{ O}$$

$$\text{empirical formula} = \boxed{\text{C}_9\text{H}_{12}\text{O}} \Rightarrow \text{empirical weight} = 136$$

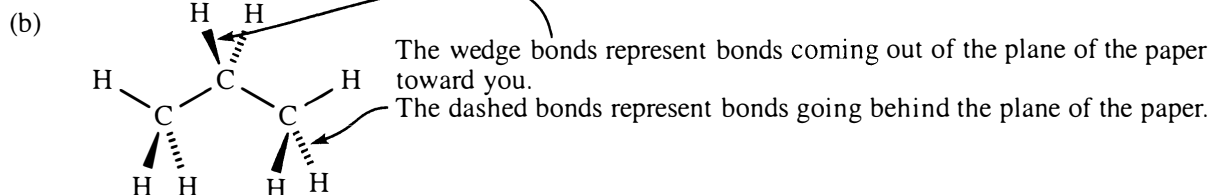
(b) molecular weight = 272, exactly twice the empirical weight

$$\text{twice the empirical formula} = \text{molecular formula} = \boxed{\text{C}_{18}\text{H}_{24}\text{O}_2}$$

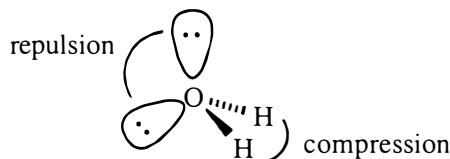
CHAPTER 2—STRUCTURE AND PROPERTIES OF ORGANIC MOLECULES

2-1 The fundamental principle of organic chemistry is that a molecule's chemical and physical properties depend on the molecule's structure: the structure-function or structure-reactivity correlation. It is essential that you understand the three-dimensional nature of organic molecules, and there is no better device to assist you than a molecular model set. You are strongly encouraged to use models regularly when reading the text and working the problems.

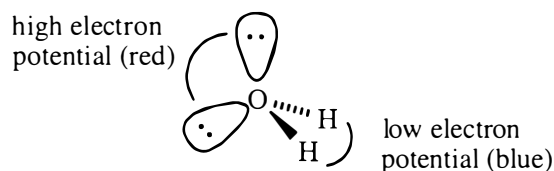
(a) requires use of models



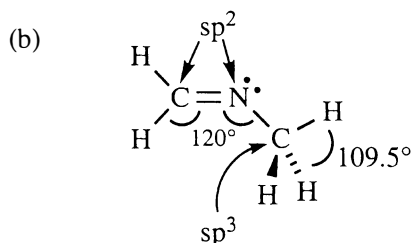
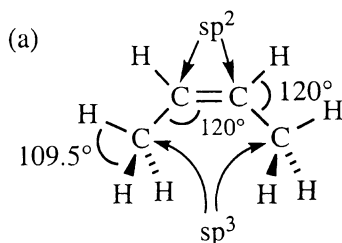
2-2 (a) The hybridization of oxygen is sp^3 since it has two sigma bonds and two pairs of nonbonding electrons. The reason that the bond angle of 104.5° is less than the perfect tetrahedral angle of 109.5° is that the lone pairs in the two sp^3 orbitals are repelling each other more strongly than the electron pairs in the sigma bonds, thereby compressing the bond angle.



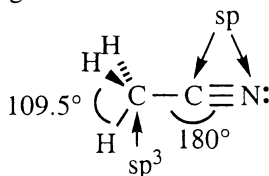
(b) The electrostatic potential map for water shows that the hydrogens have low electron potential (blue), and the area of the unshared electron pairs in sp^3 orbitals has high electron potential (red).



2-3 Each double-bonded atom is sp^2 hybridized with bond angles about 120° ; geometry around sp^2 atoms is trigonal planar. In (a), all four carbons and the two hydrogens on the sp^2 carbons are all in one plane. Each carbon on the end is sp^3 hybridized with tetrahedral geometry and bond angles about 109° . In (b), the two carbons, the nitrogen, and the two hydrogens on the sp^2 carbon are all in one plane. The CH_3 carbon is sp^3 hybridized with tetrahedral geometry and bond angles about 109° .

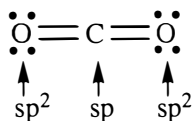


2-4 The hybridization of the nitrogen and the triple-bonded carbon are sp , giving linear geometry ($C-C-N$ are linear) and a bond angle around the triple-bonded carbon of 180° . The CH_3 carbon is sp^3 hybridized, tetrahedral, with bond angles about 109° .

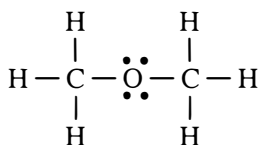


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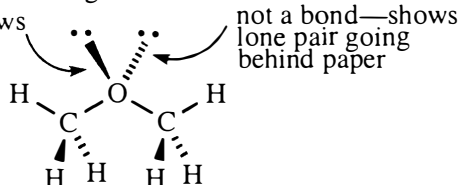
(a) linear, bond angle 180°



(b) all atoms are sp^3 ; tetrahedral geometry and bond angles of 109° around each atom

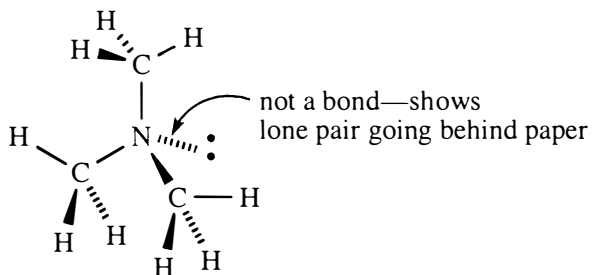
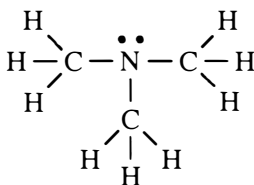


not a bond—shows lone pair coming out of paper



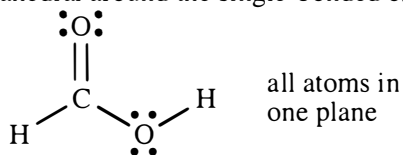
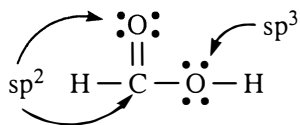
not a bond—shows lone pair going behind paper

(c) all atoms are sp^3 ; tetrahedral geometry and bond angles of 109° around each atom



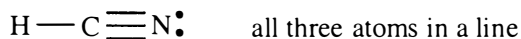
not a bond—shows lone pair going behind paper

(d) trigonal planar around the carbon, bond angles 120° ; tetrahedral around the single-bonded oxygen, bond angle 109°



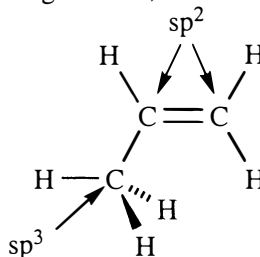
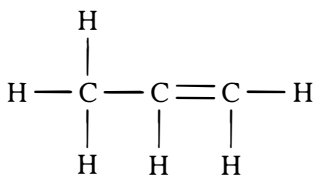
all atoms in one plane

(e) carbon and nitrogen both sp , linear, bond angle 180°

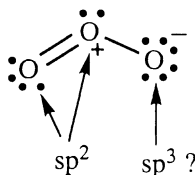
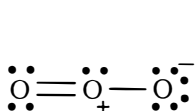


all three atoms in a line

(f) trigonal planar around the sp^2 carbons, bond angles 120° ; around the sp^3 carbon, tetrahedral geometry and 109° angles

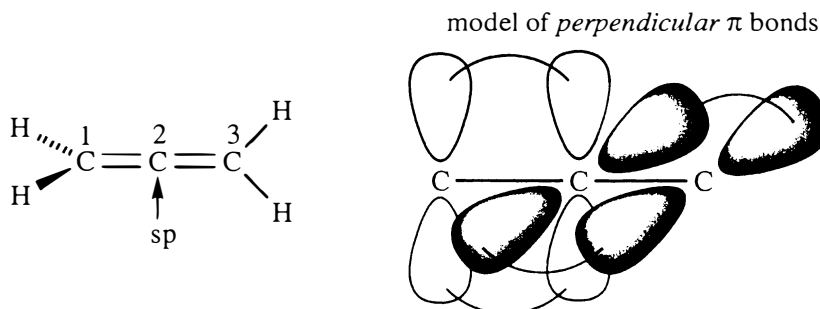


(g) trigonal planar, bond angle about 120°



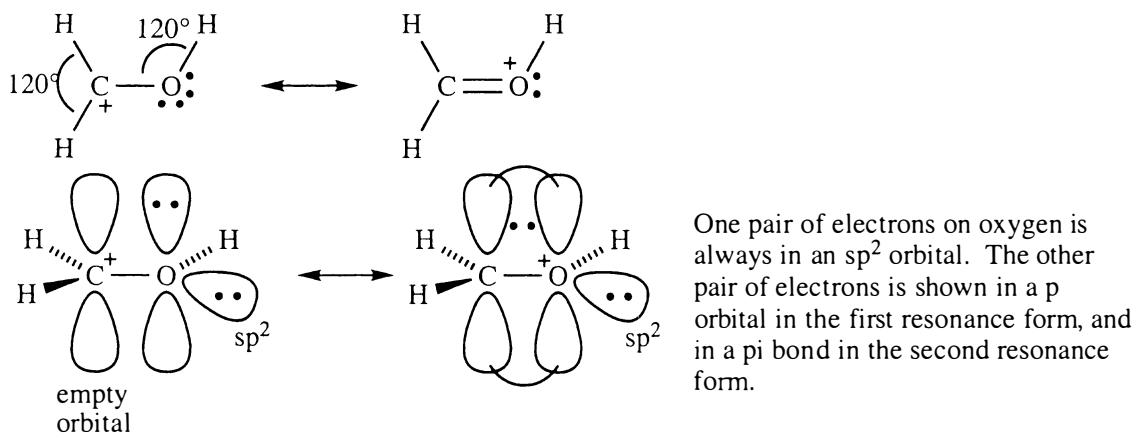
(the other resonance form of ozone shows that BOTH end oxygens must be sp^2 —see Solved Problem 2-8)

2-6 Carbon-2 is sp hybridized. If the p orbitals making the π bond between C-1 and C-2 are in the plane of the paper (putting the hydrogens in front of and behind the paper), then the other p orbital on C-2 must be perpendicular to the plane of the paper, making the π bond between C-2 and C-3 perpendicular to the paper. This necessarily places the hydrogens on C-3 in the plane of the paper. (Models will surely help.)

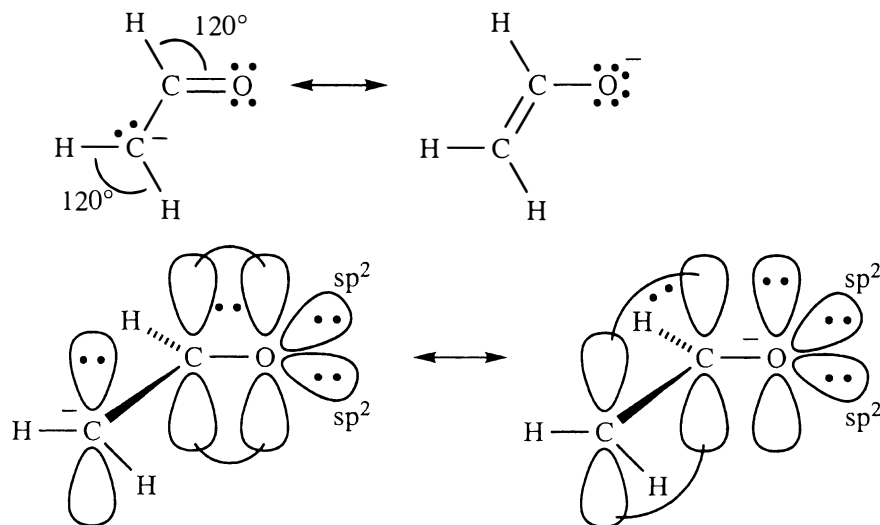


2-7 For clarity, electrons in sigma bonds are not shown.

(a) carbon and oxygen are both sp^2 hybridized

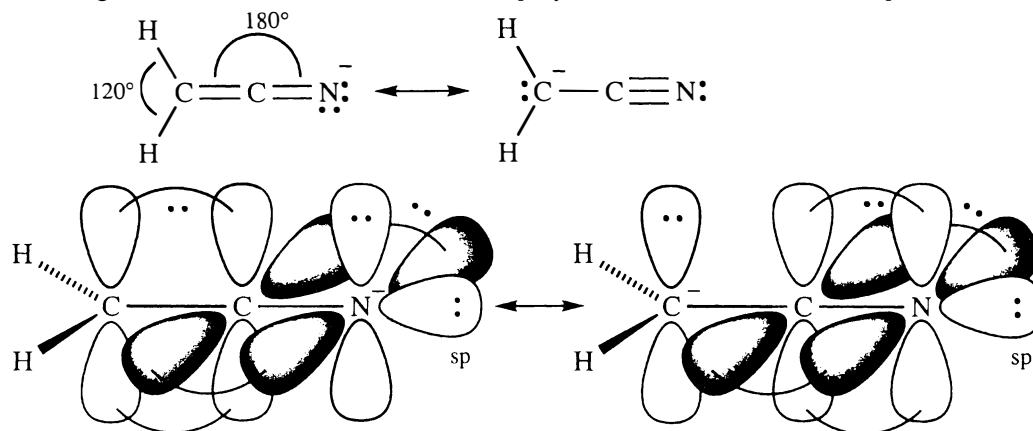


(b) oxygen and both carbons are sp^2 hybridized

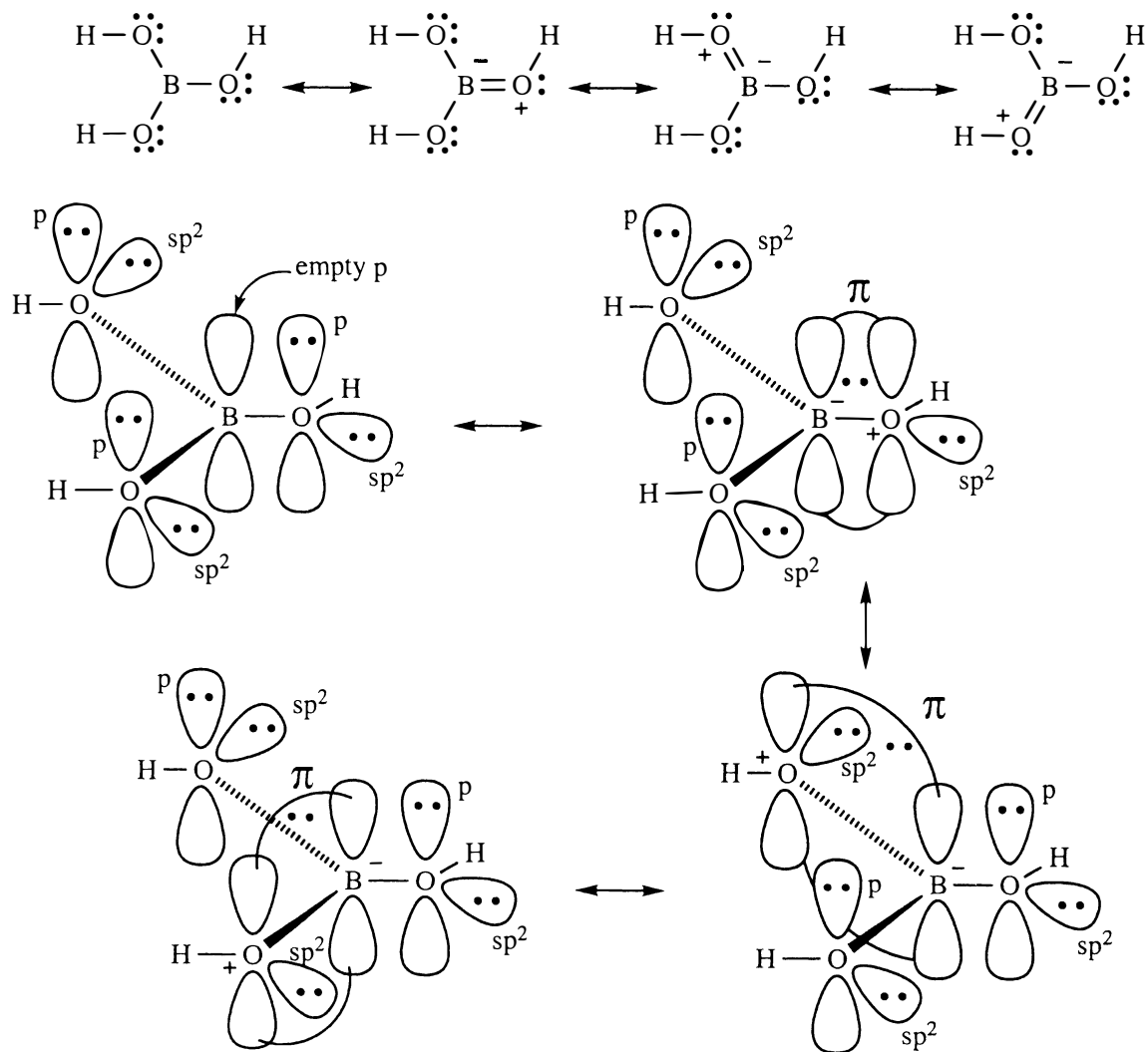


2-7 continued

(c) the nitrogen and the carbon bonded to it are sp hybridized; the left carbon is sp^2

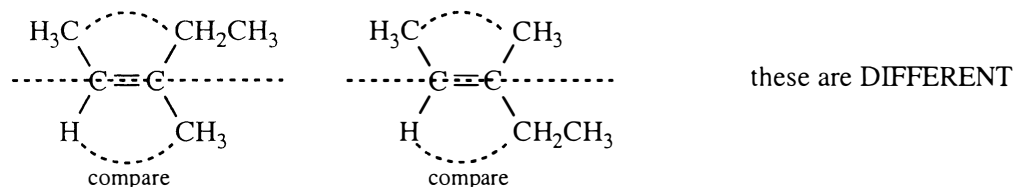


(d) the boron and the oxygens bonded to it are sp^2 hybridized



2-8 Very commonly in organic chemistry, we have to determine whether two structures are the same or different, and if they are different, what structural features are different. In order for two structures to be the same, all bonding connections have to be identical, and in the case of double bonds, the groups must be on the same side of the double bond in both structures. (A good exercise to do with your study group is to draw two structures and ask if they are the same; or draw one structure and ask how to draw a different compound.)

(a) different compounds; H and CH₃ on one carbon of the double bond, and CH₃ and CH₂CH₃ on the other carbon—same in both structures; drawing a plane through the p orbitals shows the H and CH₃ are on the same side of the double bond in the first structure, and the H and the CH₂CH₃ are on the same side in the second structure, so they are **DIFFERENT** compounds

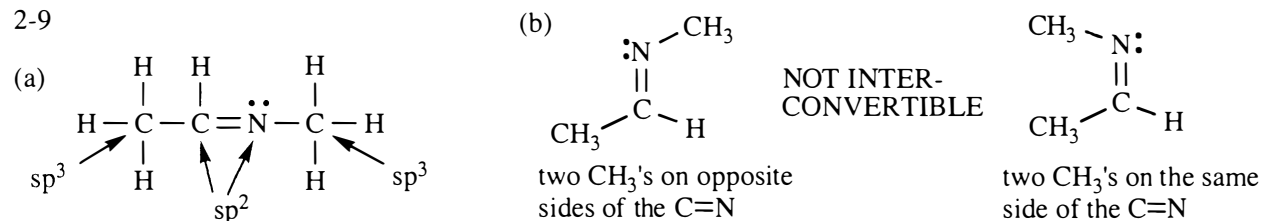


(b) same compound; in the structure on the right, the right carbon has been rotated, but the bonding is identical between the two structures

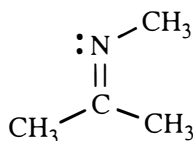
(c) different compounds; H and Br on one carbon, F and Cl on the other carbon in both structures; H and Cl on the same side of the plane through the C=C in the first structure, and H and F on the same side of the plane through the C=C in the second structure, so they are **DIFFERENT** compounds

(d) same compound: in the structure on the right, the right carbon has been rotated 120°

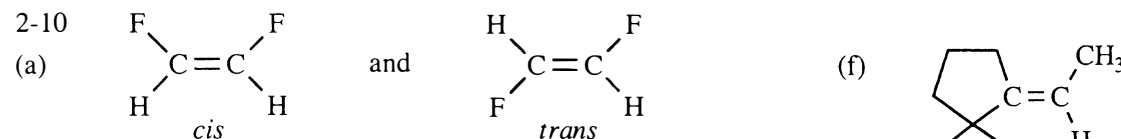
2-9



(c) the CH₃ on the N is on the same side as another CH₃ no matter how it is drawn—only one possible structure

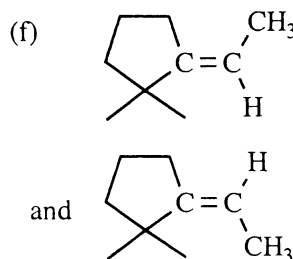
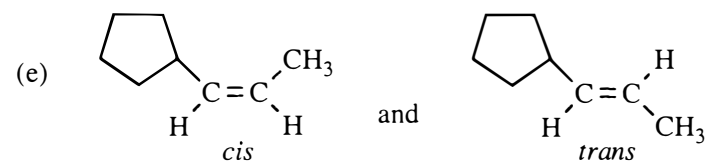


2-10



(b) no *cis-trans* isomerism
(c) no *cis-trans* isomerism
(d) no *cis-trans* isomerism

} two identical groups on one carbon of the double bond



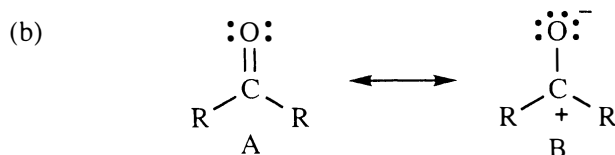
"*cis*" and "*trans*" not defined for this example

2-11 Models will be helpful here.

- (a) cis-trans isomers—the first is trans, the second is cis
- (b) constitutional isomers—the carbon skeleton is different
- (c) constitutional isomers—the bromines are on different carbons in the first structure, on the same carbon in the second structure
- (d) same compound—just flipped over
- (e) same compound—just rotated
- (f) same compound—just rotated
- (g) not isomers—different molecular formulas
- (h) constitutional isomers—the double bond has changed position
- (i) same compound—just reversed
- (j) constitutional isomers—the CH_3 groups are in different relative positions
- (k) constitutional isomers—the double bond is in a different position relative to the CH_3

2-12

- (a) $2.4 \text{ D} = 4.8 \times \delta \times 1.21 \text{ \AA}$
 $\delta = 0.41$, or 41% of a positive charge on carbon and 41% of a negative charge on oxygen



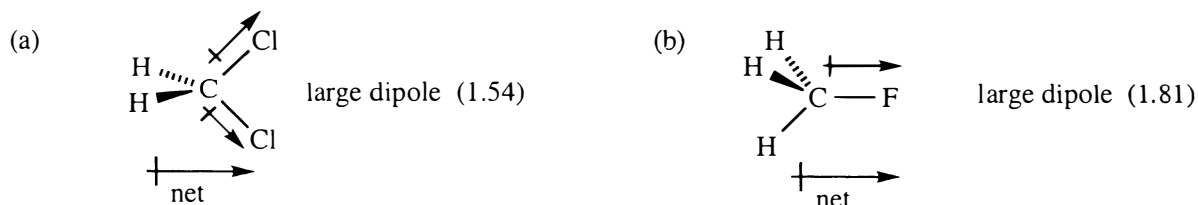
Resonance form A must be the major contributor. If B were the major contributor, the value of the charge separation would be between 0.5 and 1.0. Even though B is "minor", it is quite significant, explaining in part the high polarity of the $\text{C}=\text{O}$.

2-13

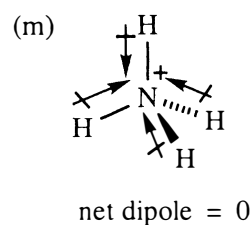
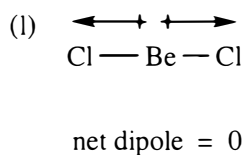
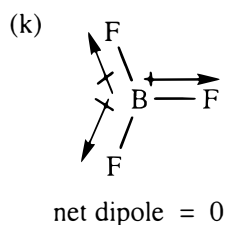
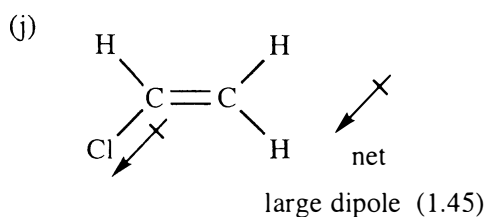
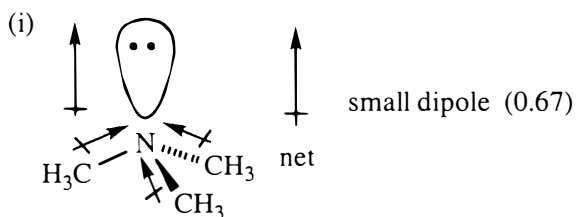
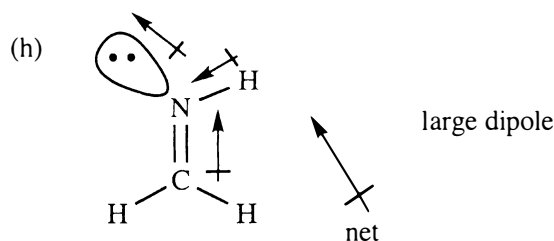
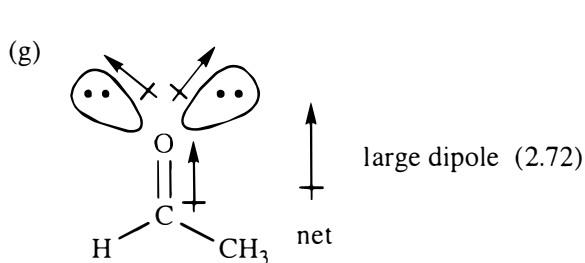
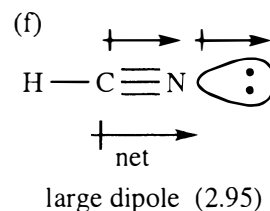
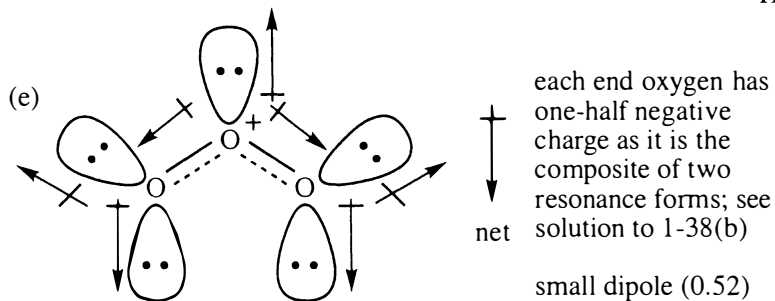
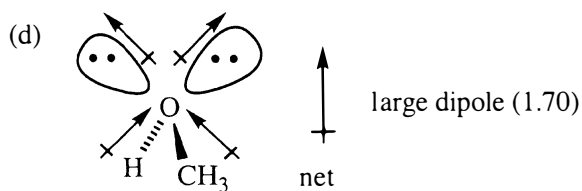
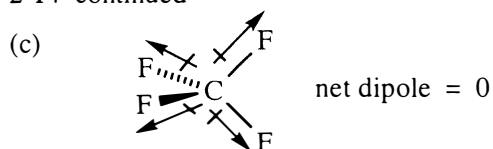
Both NH_3 and NF_3 have a pair of nonbonding electrons on the nitrogen. In NH_3 , the *direction* of polarization of the $\text{N}-\text{H}$ bonds is *toward* the nitrogen; thus, all three bond polarities and the lone pair polarity reinforce each other. In NF_3 , on the other hand, the direction of polarization of the $\text{N}-\text{F}$ bonds is *away from* the nitrogen; the three bond polarities cancel the lone pair polarity, so the net result is a very small *molecular* dipole moment.



2-14 Some magnitudes of dipole moments are difficult to predict; however, the direction of the dipole should be straightforward, in most cases. Actual values of molecular dipole moments are given in parentheses. (Each halogen atom has three nonbonded electron pairs, not shown below.) The $\text{C}-\text{H}$ is usually considered non-polar.

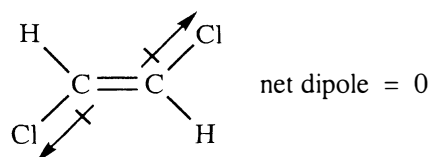
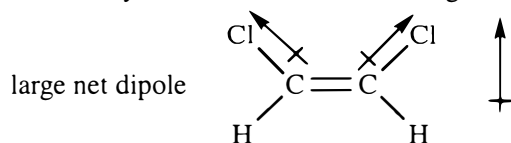


2-14 continued

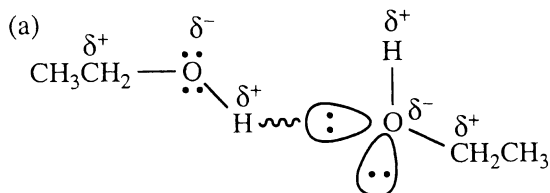


In (k) through (m), the symmetry of the molecule allows the individual bond dipoles to cancel.

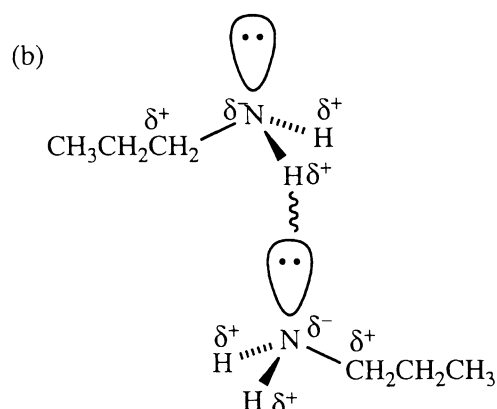
2-15 With chlorines on the same side of the double bond, the bond dipole moments reinforce each other, resulting in a large net dipole. With chlorines on opposite sides of the double bond, the bond dipole moments exactly cancel each other, resulting in a zero net dipole.



2-16



(hydrogen bonds shown as wavy bond)



2-17

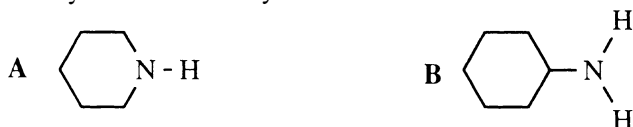
(a) $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$ has less branching and boils at a higher temperature than $(\text{CH}_3)_3\text{CC}(\text{CH}_3)_3$.

(b) $\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH}$ can form hydrogen bonds and will boil at a much higher temperature than $\text{CH}_3(\text{CH}_2)_6\text{CH}_3$ which cannot form hydrogen bonds.

(c) $\text{HOCH}_2(\text{CH}_2)_4\text{CH}_2\text{OH}$ can form hydrogen bonds at both ends and has no branching; it will boil at a much higher temperature than $(\text{CH}_3)_3\text{CCH}(\text{OH})\text{CH}_3$.

(d) $(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{NH}$ has an N—H bond and can form hydrogen bonds; it will boil at a higher temperature than $(\text{CH}_3\text{CH}_2)_3\text{N}$ which cannot form hydrogen bonds.

(e) The second compound shown (**B**) has the higher boiling point for two reasons: **B** has a higher molecular weight than **A**; and **B**, a primary amine with two N—H bonds, has more opportunity for forming hydrogen bonds than **A**, a secondary amine with only one N—H bond.



2-18

(a) $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ can form hydrogen bonds with water and is more soluble than $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ which cannot form hydrogen bonds with water.

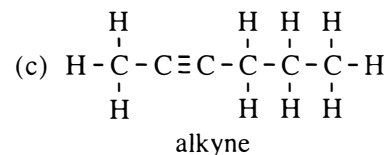
(b) $\text{CH}_3\text{CH}_2\text{NHCH}_3$ is more water soluble because it can form hydrogen bonds; $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ cannot form hydrogen bonds.

(c) $\text{CH}_3\text{CH}_2\text{OH}$ is more soluble in water. The polar O—H group forms hydrogen bonds with water, overcoming the resistance of the non-polar CH_3CH_2 group toward entering the water. In $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$, however, the hydrogen bonding from only one OH group cannot carry a four-carbon chain into the water; this substance is only slightly soluble in water.

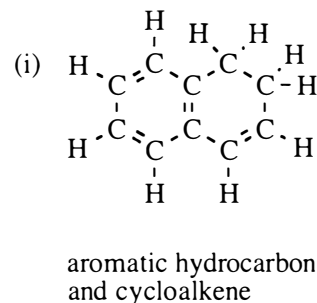
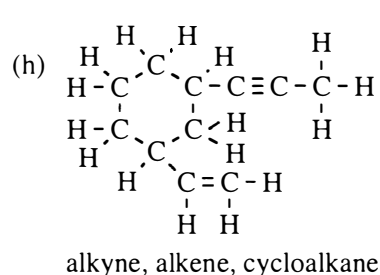
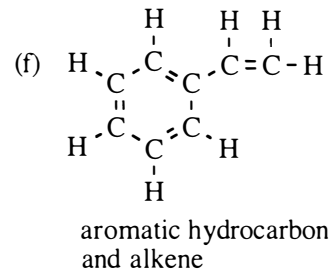
(d) Both compounds form hydrogen bonds with water at the double-bonded oxygen, but only the smaller molecule (CH_3COCH_3) dissolves. The cyclic compound has too many non-polar CH_2 groups to dissolve.

(a)
$$\begin{array}{ccccccc} & \text{H} & \text{H} & \text{H} & \text{H} & \text{H} & \\ & | & | & | & | & | & \\ \text{H} & - \text{C} & - \text{C} & - \text{C} & - \text{C} & - \text{C} & - \text{H} \\ & | & | & | & | & | & \\ & \text{H} & \text{H} & \text{H} & \text{H} & \text{H} & \end{array}$$

alkane

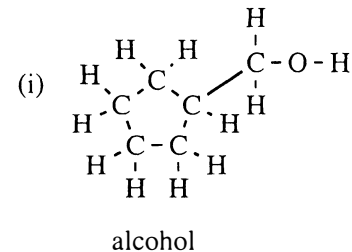
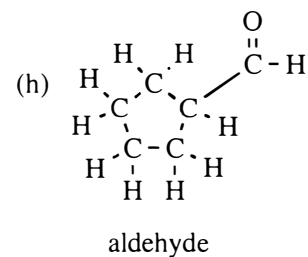
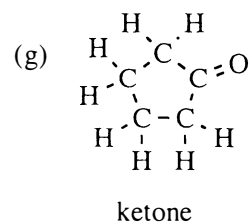
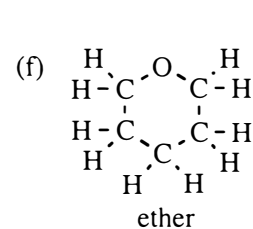
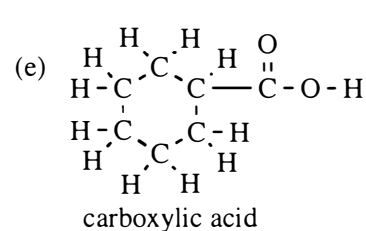
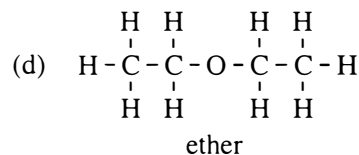
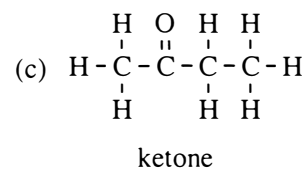
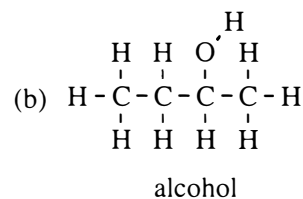


(d) 

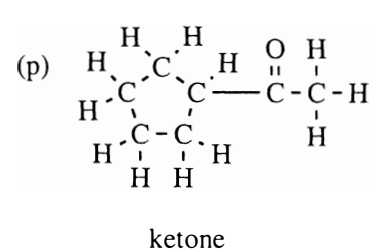
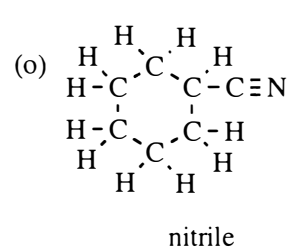
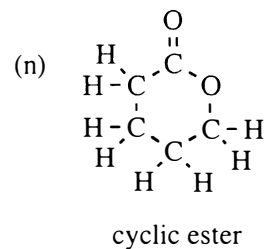
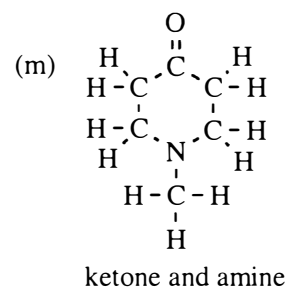
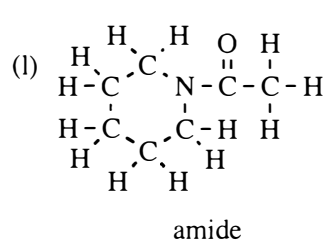
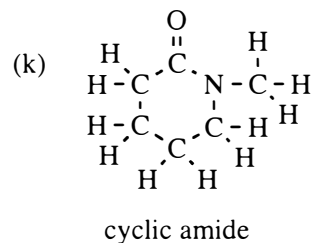
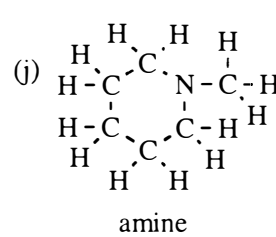
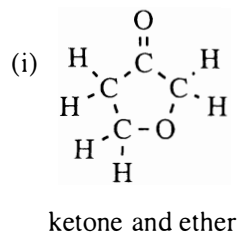
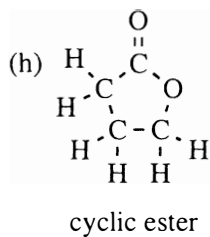
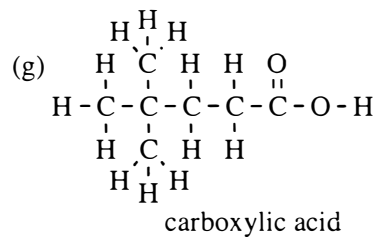
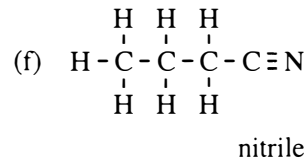
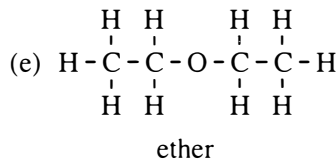
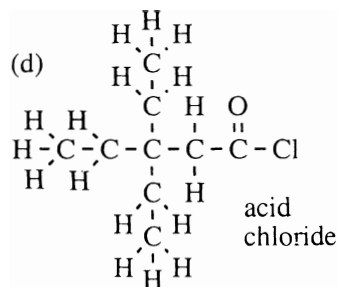
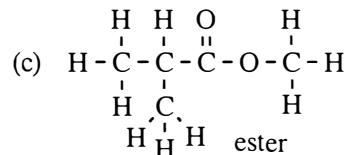
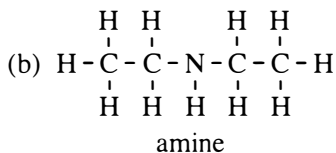
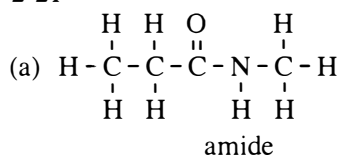


(a)
$$\begin{array}{ccccccc} & & \text{H} & & \text{H} & & \text{O} \\ & & | & & | & & || \\ \text{(a)} & \text{H} & - \text{C} & - & \text{C} & - & \text{C} - \text{H} \\ & & | & & | & & \\ & & \text{H} & & \text{H} & & \end{array}$$

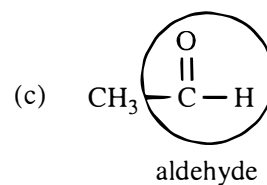
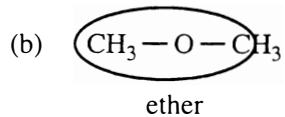
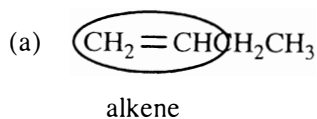
aldehyde



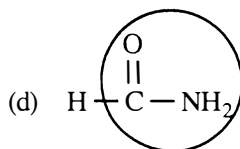
2-21



2-22 When the identity of a functional group depends on several atoms, all of those atoms should be circled. For example, an ether is an oxygen between two carbons, so the oxygen and both carbons should be circled. A ketone is a carbonyl group between two other carbons, so all those atoms should be circled.

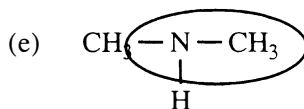


2-22 continued

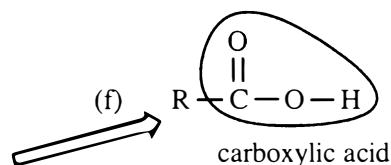


amide

(this also looks like an aldehyde, but an amide has higher "priority" as you will see later)

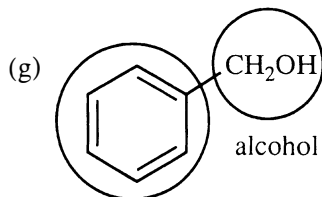


amine



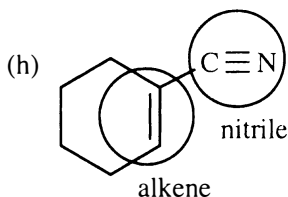
carboxylic acid

Suggested by student Richard King: R is the symbol that organic chemists use to represent alkyl and aryl groups. As you will see in the course of your study, there are quite a few ways that carbon and hydrogen atoms can go together to form alkyl and aryl groups. So when you see this symbol, you should know that it represents ONLY some combination of carbon and hydrogen atoms—except when it includes other atoms.



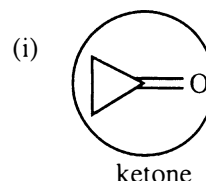
alcohol

aromatic

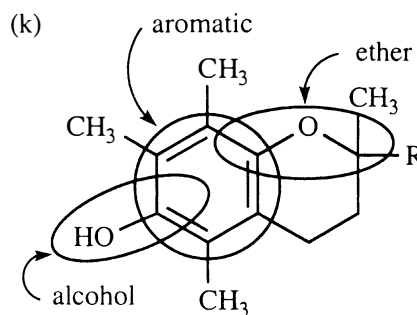
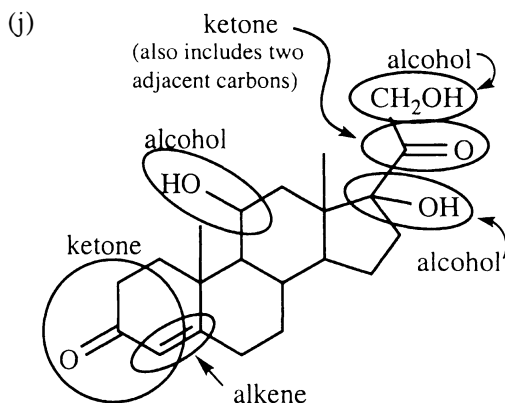


nitrile

alkene



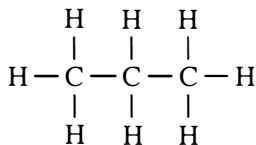
ketone



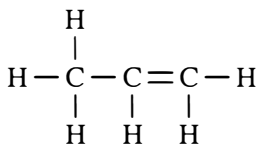
2-23 Please refer to solution 1-20, page 12 of this Solutions Manual.

2-24 The examples here are representative. Your examples may be different and still correct. What is important in this problem is to have the same functional group.

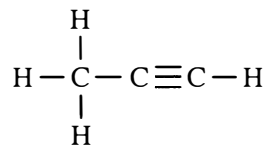
(a) alkane: hydrocarbon with all single bonds; can be acyclic (no ring) or cyclic



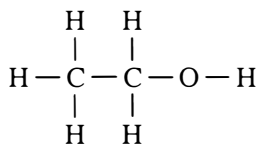
(b) alkene: contains a carbon-carbon double bond



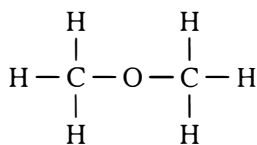
(c) alkyne: contains a carbon-carbon triple bond



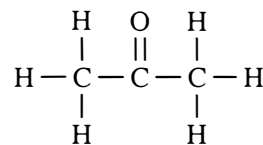
(d) alcohol: contains an OH group on a carbon



(e) ether: contains an oxygen between two carbons

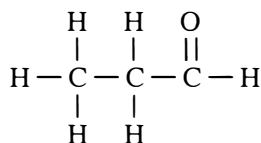


(f) ketone: contains a carbonyl group between two carbons

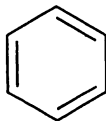


2-24 continued

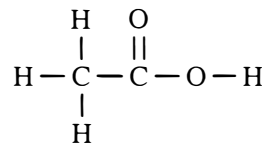
(g) aldehyde: contains a carbonyl group with a hydrogen on one side



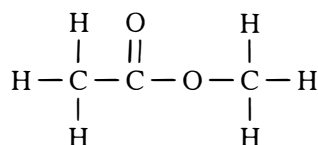
(h) aromatic hydrocarbon: a cyclic hydrocarbon with alternating double and single bonds



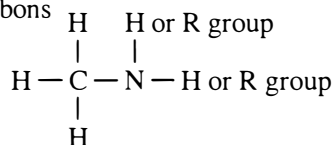
(i) carboxylic acid: contains a carbonyl group with an OH group on one side



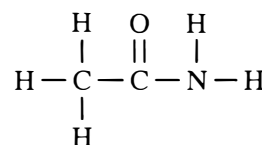
(j) ester: contains a carbonyl group with an O—C on one side



(k) amine: contains a nitrogen bonded to one, two, or three carbons



(l) amide: contains a carbonyl group with a nitrogen on one side

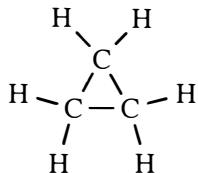


(m) nitrile: contains the carbon-nitrogen triple bond: $\text{H}_3\text{C}-\text{C}\equiv\text{N}$

2-25 Models show that the tetrahedral geometry of CH_2Cl_2 precludes stereoisomers.

2-26

(a)

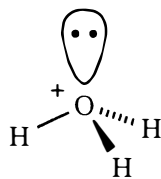


(b) Cyclopropane must have 60° bond angles compared with the usual sp^3 bond angle of 109.5° in an acyclic molecule.

(c) Like a bent spring, bonds that deviate from their normal angles or positions are highly strained. Cyclopropane is reactive because breaking the ring relieves the strain.

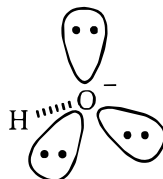
2-27

(a)



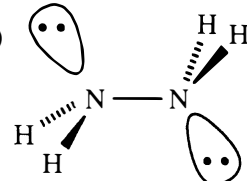
sp^3 , $\approx 109^\circ$

(b)



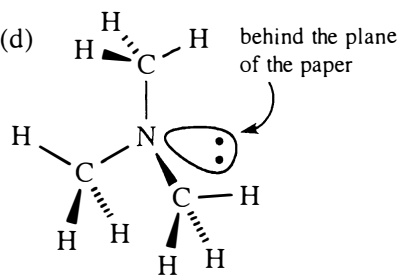
sp^3 , no bond angle because oxygen is bonded to only one atom

(c)



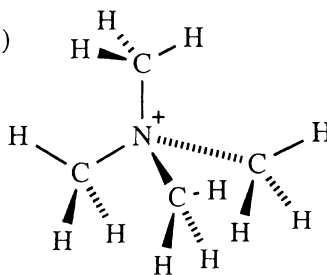
both sp^3 , all $\approx 109^\circ$

(d)



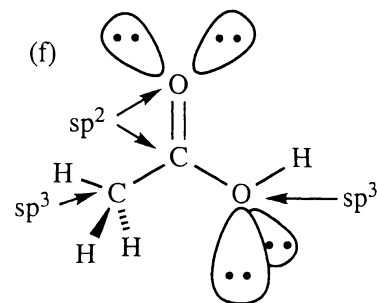
all sp^3 , all $\approx 109^\circ$

(e)



all sp^3 , all $\approx 109^\circ$

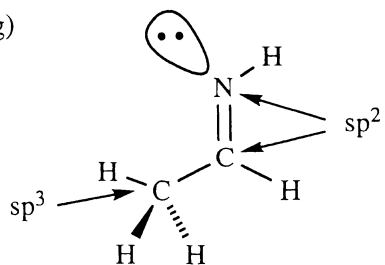
(f)



angles around sp^3 atoms $\approx 109^\circ$
angles around sp^2 carbon $\approx 120^\circ$

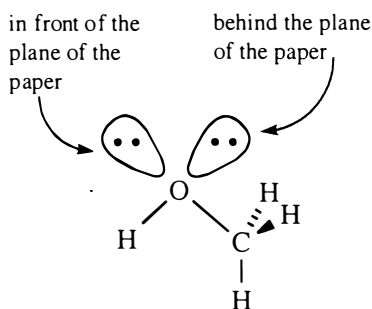
2-27 continued

(g)



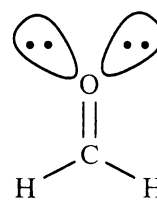
angles around sp^3 atom $\approx 109^\circ$
angles around sp^2 atoms $\approx 120^\circ$

(h)



both sp^3 , all $\approx 109^\circ$

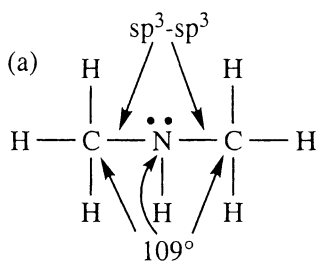
(i)



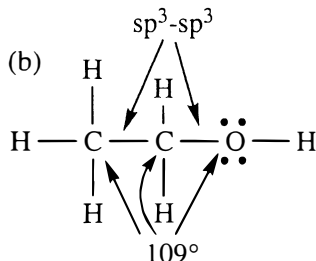
both sp^2 , all $\approx 120^\circ$

2-28 For clarity in these pictures, bonds between hydrogen and an sp^3 atom are not labeled; these bonds are $s-sp^3$ overlap.

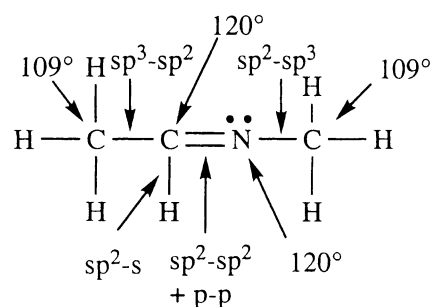
(a)



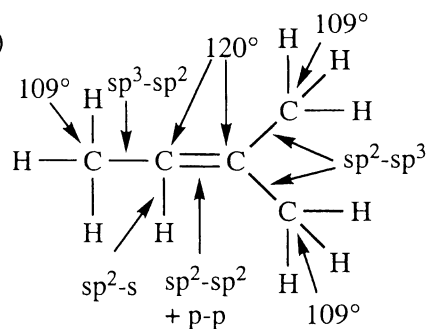
(b)



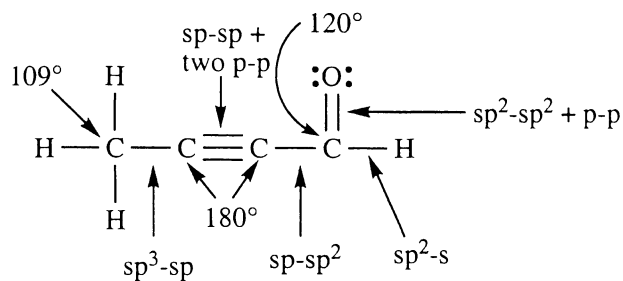
(c)



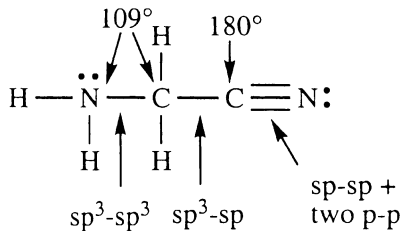
(d)



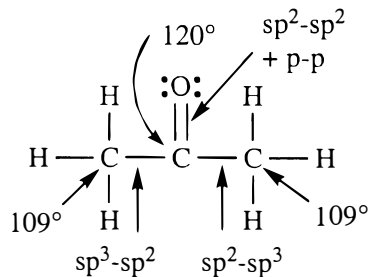
(e)



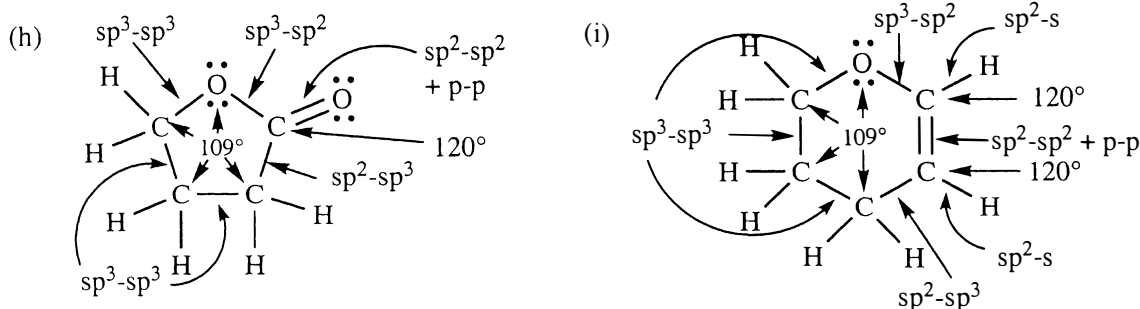
(f)



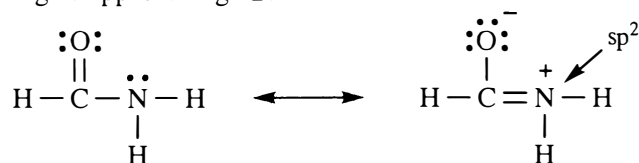
(g)



2-28 continued

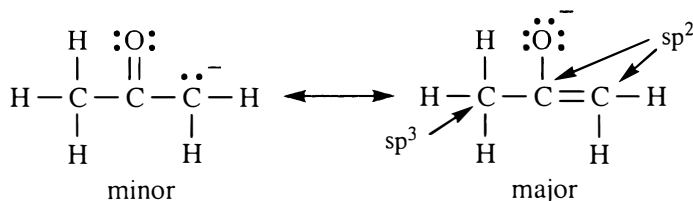


2-29 The second resonance form of formamide is a minor but significant resonance contributor. It shows that the nitrogen-carbon bond has some double bond character, requiring that the nitrogen be sp^2 hybridized with bond angles approaching 120° .

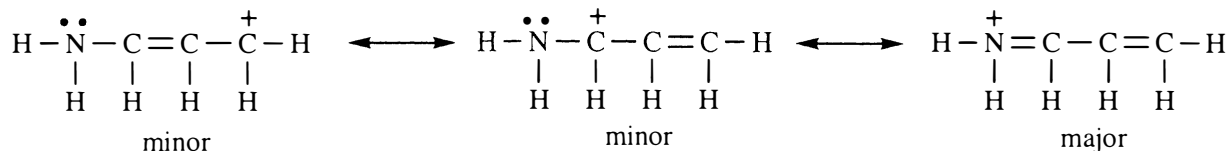


2-30

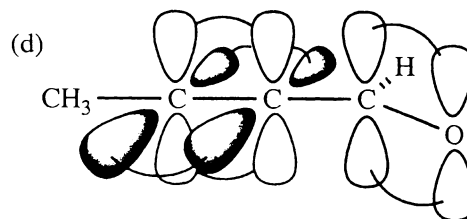
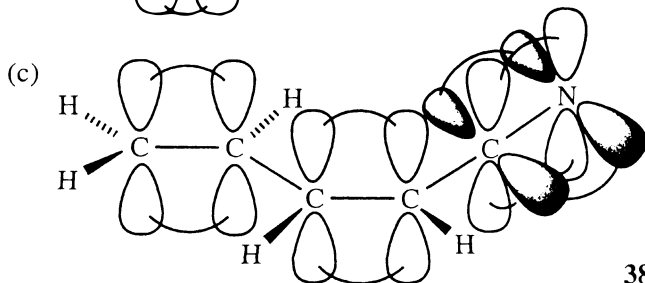
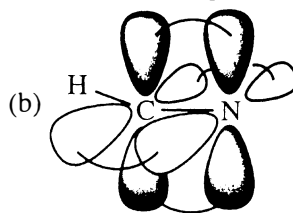
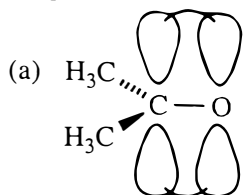
(a) The major resonance contributor shows a carbon-carbon double bond, suggesting that both carbons are sp^2 hybridized with trigonal planar geometry. The CH_3 carbon is sp^3 hybridized with tetrahedral geometry.



(b) The major resonance contributor shows a carbon-nitrogen double bond, suggesting that all three carbons and the nitrogen are sp^2 hybridized with trigonal planar geometry.

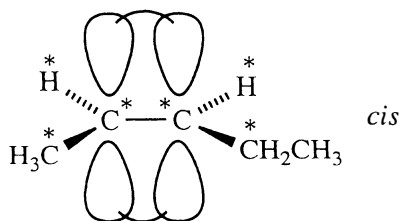


2-31 In (c) and (d), the unshadowed p orbitals are vertical and parallel. The shadowed p orbitals are perpendicular and horizontal.



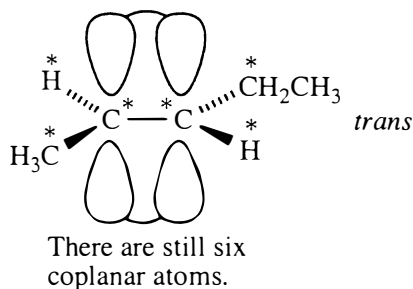
2-32

(a)

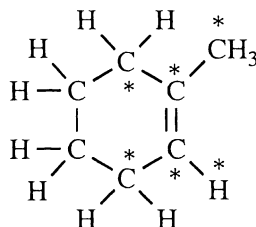


(b) The coplanar atoms in the structures to the left and below are marked with asterisks.

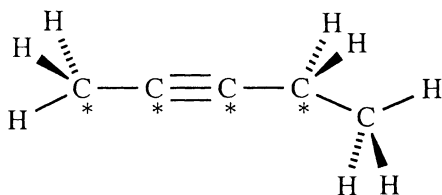
(c)



(d)



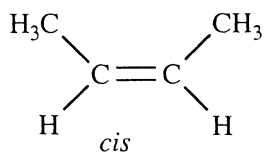
2-33 Collinear atoms are marked with asterisks.



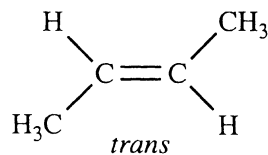
2-34

(a) no *cis-trans* isomerism

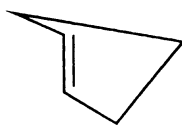
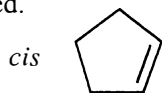
(b)



and

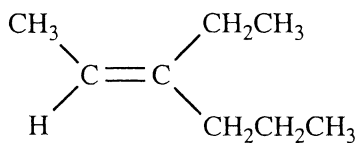
(c) no *cis-trans* isomerism

(d) Theoretically, cyclopentene could show *cis-trans* isomerism. In reality, the *trans* form is too unstable to exist because of the necessity of stretched bonds and deformed bond angles. *trans*-Cyclopentene has never been detected.

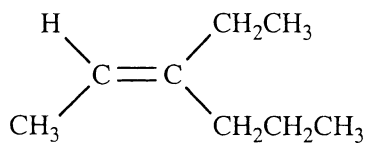


"*trans*"—not possible because of ring strain

(e)



and

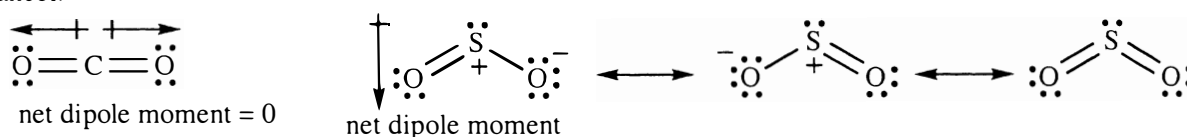


these are *cis-trans* isomers, but the designation of *cis* and *trans* to specific structures is not defined because of four different groups on the double bond

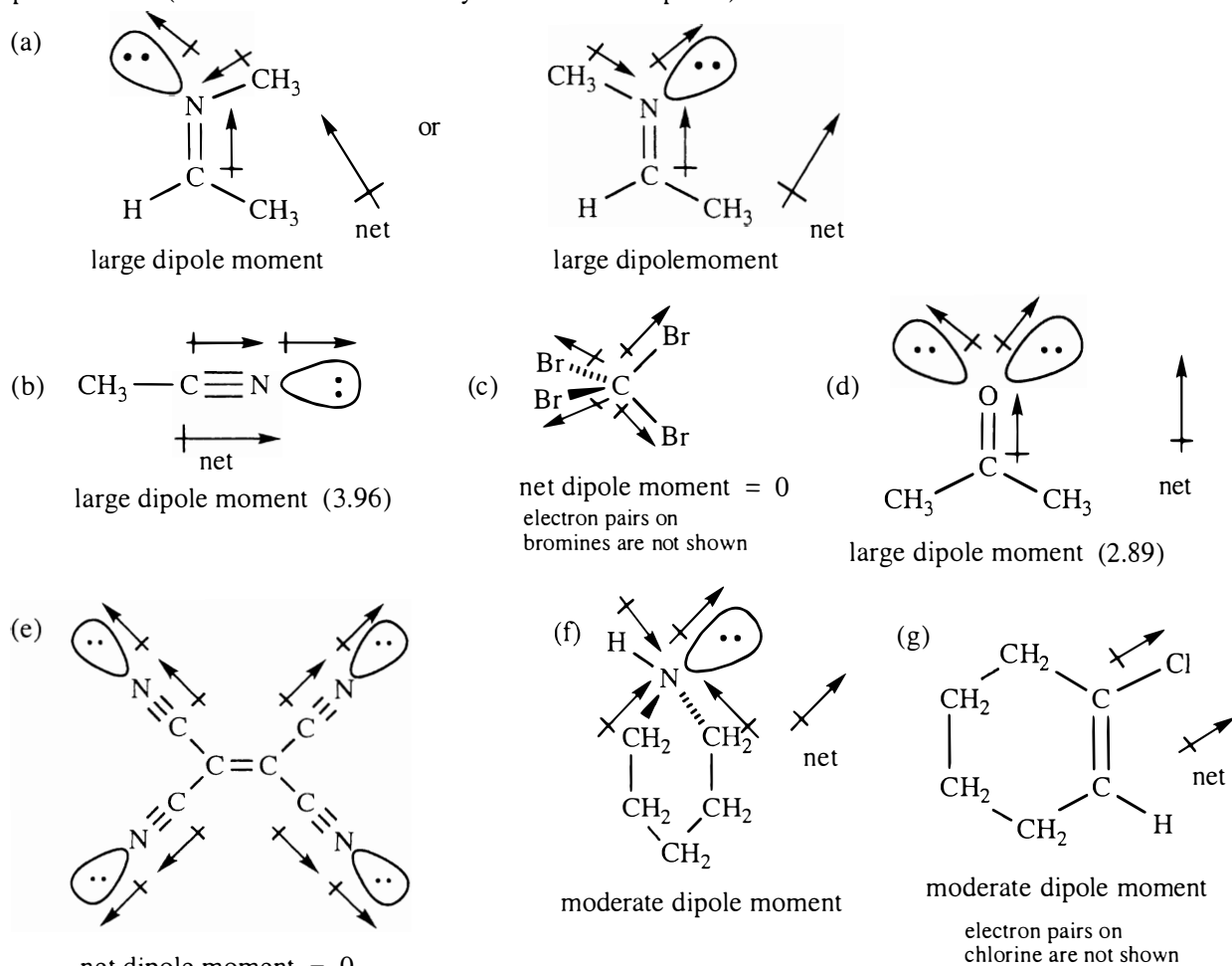
2-35

- (a) constitutional isomers—the carbon skeletons are different
- (b) constitutional isomers—the position of the chlorine atom has changed
- (c) cis-trans isomers—the first is *cis*, the second is *trans*
- (d) constitutional isomers—the carbon skeletons are different
- (e) cis-trans isomers—the first is *trans*, the second is *cis*
- (f) same compound—rotation of the first structure gives the second
- (g) cis-trans isomers—the first is *cis*, the second is *trans*
- (h) constitutional isomers—the position of the double bond relative to the ketone has changed (while it is true that the first double bond is *cis* and the second is *trans*, in order to have *cis-trans* isomers, the rest of the structure must be identical)

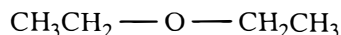
2-36 CO_2 is linear; its bond dipoles cancel, so it has no net dipole. SO_2 is bent, so its bond dipoles do not cancel.



2-37 Some magnitudes of dipole moments are difficult to predict; however, the direction of the dipole should be straightforward in most cases. Actual values of molecular dipole moments are given in parentheses. (The C—H bond is usually considered non-polar.)

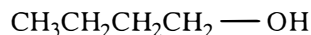


2-38 Diethyl ether and 1-butanol each have one oxygen, so each can form hydrogen bonds with water (water supplies the H for hydrogen bonding with diethyl ether); their water solubilities should be similar. The boiling point of 1-butanol is much higher because these molecules can hydrogen bond with each other, thus requiring more energy to separate one molecule from another. Diethyl ether molecules cannot hydrogen bond with each other, so it is relatively easy to separate them.



diethyl ether

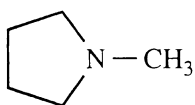
can hydrogen bond with water
cannot hydrogen bond with itself



1-butanol

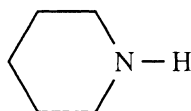
can hydrogen bond with water
can hydrogen bond with itself

2-39



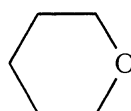
N-methylpyrrolidine

b.p. 81°C



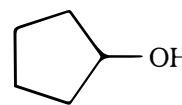
piperidine

b.p. 106°C



tetrahydropyran

b.p. 88°C



cyclopentanol

b.p. 141°C

(a) Piperidine has an N—H bond, so it can hydrogen bond with other molecules of itself.

N-Methylpyrrolidine has no N—H, so it cannot hydrogen bond and will require less energy (lower boiling point) to separate one molecule from another.

(b) Two effects need to be explained: 1) Why does cyclopentanol have a higher boiling point than tetrahydropyran? and 2) Why do the oxygen compounds have a greater difference in boiling points than the analogous nitrogen compounds?

The answer to the first question is the same as in (a): cyclopentanol can hydrogen bond with its neighbors while tetrahydropyran cannot.

The answer to the second question lies in the text, Table 2-1, that shows the bond dipole moments for C—O and H—O are much greater than C—N and H—N; bonds to oxygen are more polarized, with greater charge separation than bonds to nitrogen.

How is this reflected in the data? The boiling points of tetrahydropyran (88°C) and *N*-methylpyrrolidine (81°C) are close; tetrahydropyran molecules would have a slightly stronger dipole-dipole attraction, and tetrahydropyran is a little less "branched" than *N*-methylpyrrolidine, so it is reasonable that tetrahydropyran boils at a slightly higher temperature. The large difference comes when comparing the boiling points of cyclopentanol (141°C) and piperidine (106°C). The greater polarity of O—H versus N—H is reflected in a more negative oxygen (more electronegative than nitrogen) and a more positive hydrogen, resulting in a much stronger intermolecular attraction. The conclusion is that hydrogen bonding due to O—H is much stronger than that due to N—H.

2-40

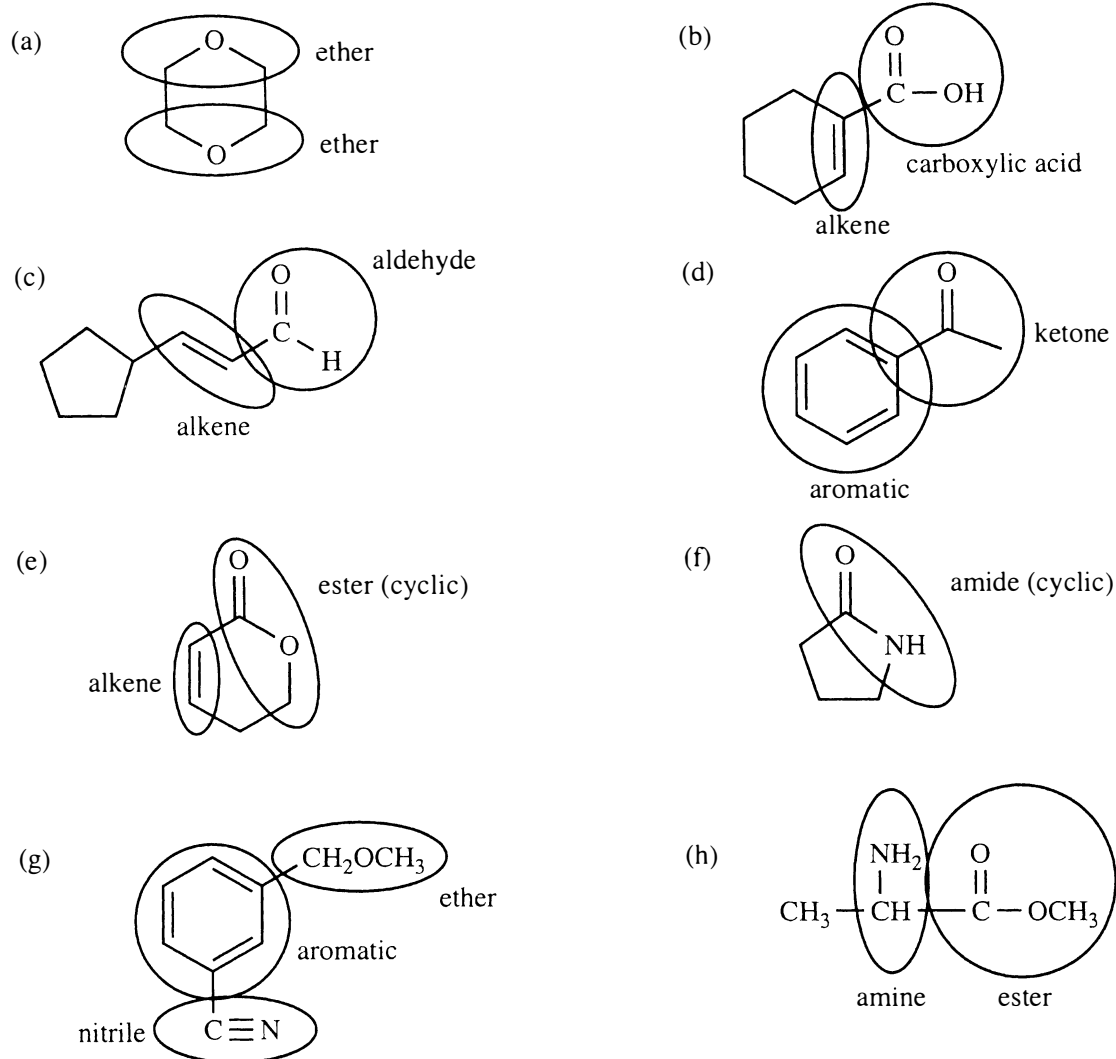
- (a) can hydrogen bond with itself and with water
- (b) can hydrogen bond only with water
- (c) can hydrogen bond with itself and with water
- (d) can hydrogen bond only with water
- (e) cannot hydrogen bond
- (f) cannot hydrogen bond

- (g) can hydrogen bond only with water
- (h) can hydrogen bond with itself and with water
- (i) can hydrogen bond only with water
- (j) can hydrogen bond only with water
- (k) can hydrogen bond only with water
- (l) can hydrogen bond with itself and with water

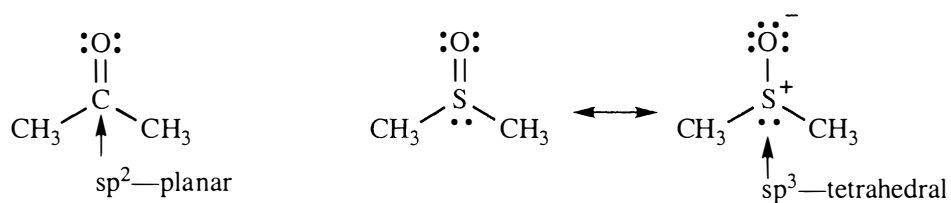
2-41 Higher-boiling compounds are listed.

- (a) $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$ can form hydrogen bonds with other identical molecules
- (b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ has a higher molecular weight than $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$
- (c) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ has less branching than $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_3$
- (d) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$ has a higher molecular weight AND dipole-dipole interaction compared with $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$

2-42

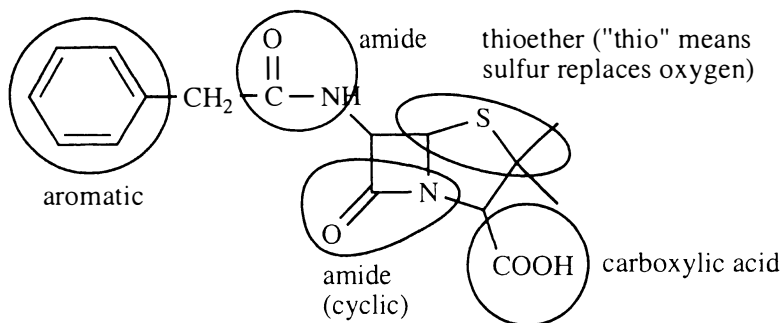


2-43

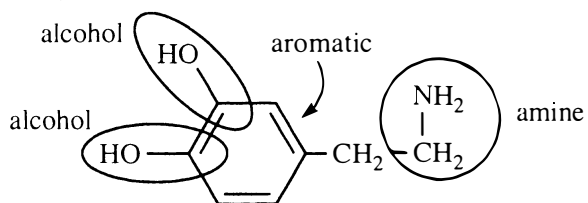


The key to this problem is understanding that sulfur has a *lone pair of electrons*. The second resonance form shows four pairs of electrons around the sulfur atom, an electronic configuration requiring sp^3 hybridization. Sulfur in DMSO cannot be sp^2 like carbon in acetone, so we would expect sulfur's geometry to be pyramidal (the four electron pairs around sulfur require tetrahedral geometry, but the three atoms around sulfur define its shape as pyramidal).

(a) penicillin G

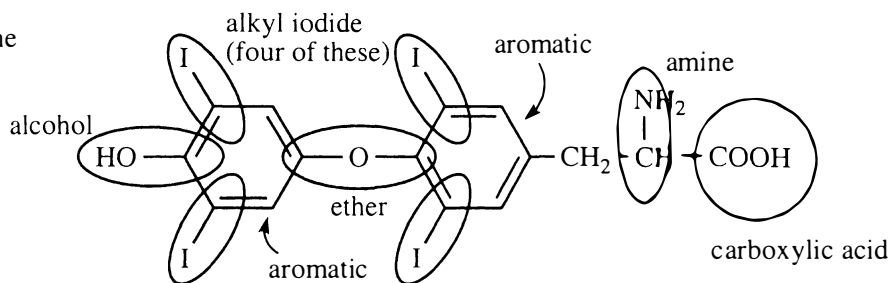


(b) dopamine

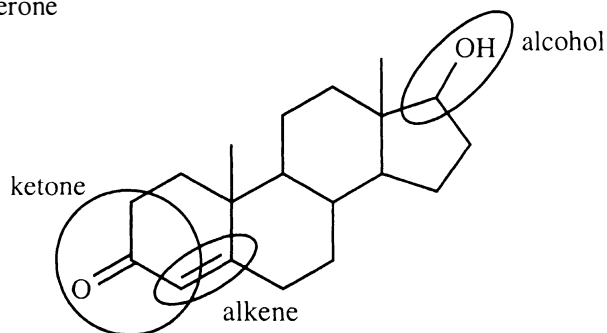


(In later chapters, you will learn that the OH group on a benzene ring is a special functional group called a "phenol". For now, it fits the broad definition of an alcohol.)

(c) thyroxine



(d) testosterone



CHAPTER 3—STRUCTURE AND STEREOCHEMISTRY OF ALKANES

3-1

(a) C_nH_{2n+2} where $n = 25$ gives $C_{25}H_{52}$

(b) C_nH_{2n+2} where $n = 44$ gives $C_{44}H_{90}$

Note to the student: The IUPAC system of nomenclature has a well defined set of rules determining how structures are named. You will find a summary of these rules as Appendix 1 in this Solutions Manual.

3-2 Use hyphens to separate letters from numbers. Longest chains may not always be written left to right.

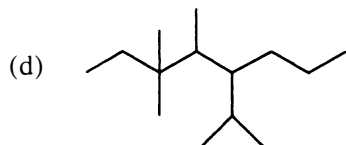
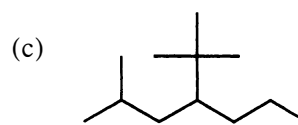
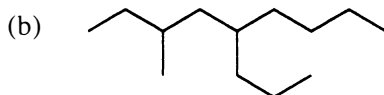
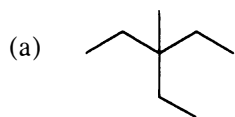
(a) 3-methylpentane (always find the longest chain; it may not be written in a straight line)

(b) 2-bromo-3-methylpentane (always find the longest chain)

(c) 5-ethyl-2-methyl-4-propylheptane ("When there are two longest chains of equal length, use the chain with the greater number of substituents.")

(d) 4-isopropyl-2-methyldecane

3-3 This Solutions Manual will present line formulas where a question asks for an answer including a structure. If you use condensed structural formulas instead, be sure that you are able to "translate" one structure type into the other.



3-4 Separate numbers from numbers with commas.

(a) 2-methylbutane

(c) 3-ethyl-2-methylhexane

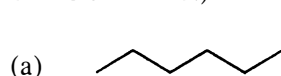
(e) 3-ethyl-2,2,4,5-tetramethylhexane

(b) 2,2-dimethylpropane

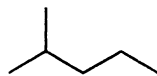
(d) 2,4-dimethylhexane

(f) 4-*t*-butyl-3-methylheptane

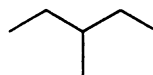
3-5 (Hints: *systematize* your approach to these problems. For the isomers of a six carbon formula, for example, start with the isomer containing all six carbons in a straight chain, then the isomers containing a five-carbon chain, then a four-carbon chain, *etc.* Carefully check your answers to AVOID DUPLICATE STRUCTURES.)



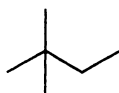
n-hexane



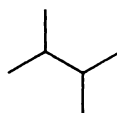
2-methylpentane



3-methylpentane



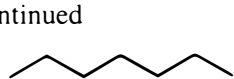
2,2-dimethylbutane



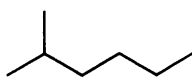
2,3-dimethylbutane

3-5 continued

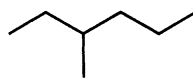
(b)



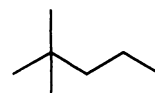
n-heptane



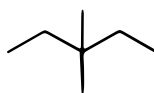
2-methylhexane



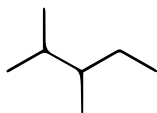
3-methylhexane



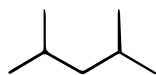
2,2-dimethylpentane



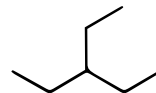
3,3-dimethylpentane



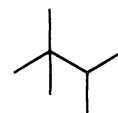
2,3-dimethylpentane



2,4-dimethylpentane



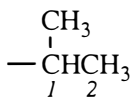
3-ethylpentane



2,2,3-trimethylbutane

3-6 For this problem, the carbon numbers in the substituents are indicated in italics.

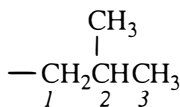
(a)



1-methylethyl

common name = isopropyl

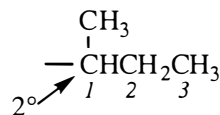
(b)



2-methylpropyl

common name = isobutyl

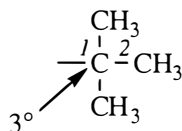
(c)



1-methylpropyl

common name = *sec*-butyl

(d)

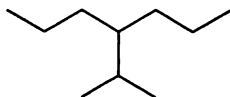


1,1-dimethylethyl

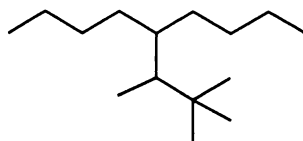
common name = *t*-butyl or *tert*-butyl

3-7

(a)



(b)



3-8 Once the number of carbons is determined, C_nH_{2n+2} gives the formula.

(a) $C_{10}H_{22}$

(b) $C_{15}H_{32}$

3-9

(a) (lowest b.p.) hexane < octane < decane (highest b.p.) —molecular weight

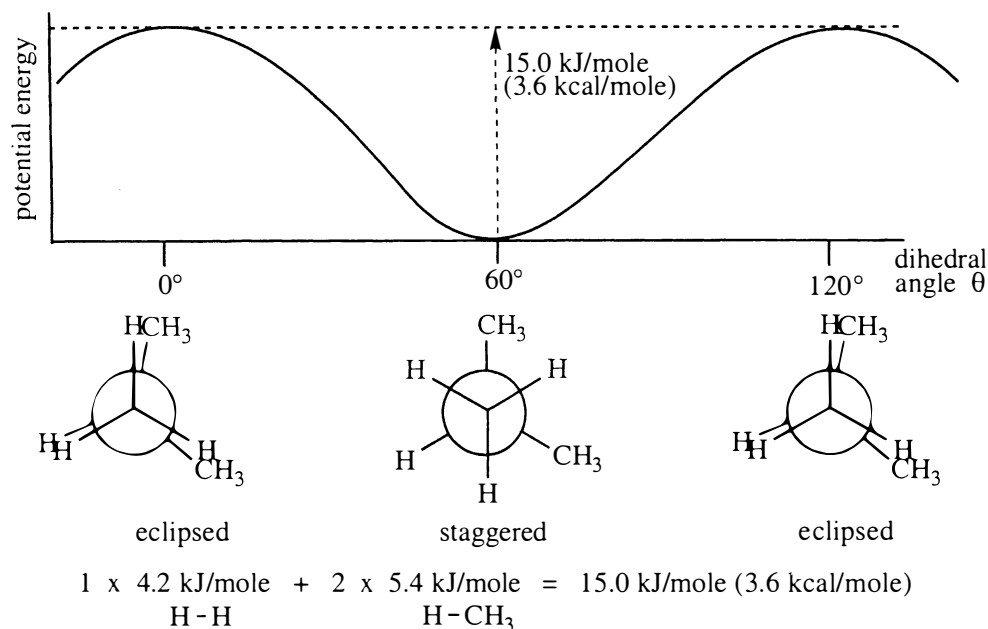
(b) $(CH_3)_3C-C(CH_3)_3 < CH_3CH_2C(CH_3)_2CH_2CH_2CH_3 < \text{octane}$ —branching
(lowest b.p.) (highest b.p.)

3-10

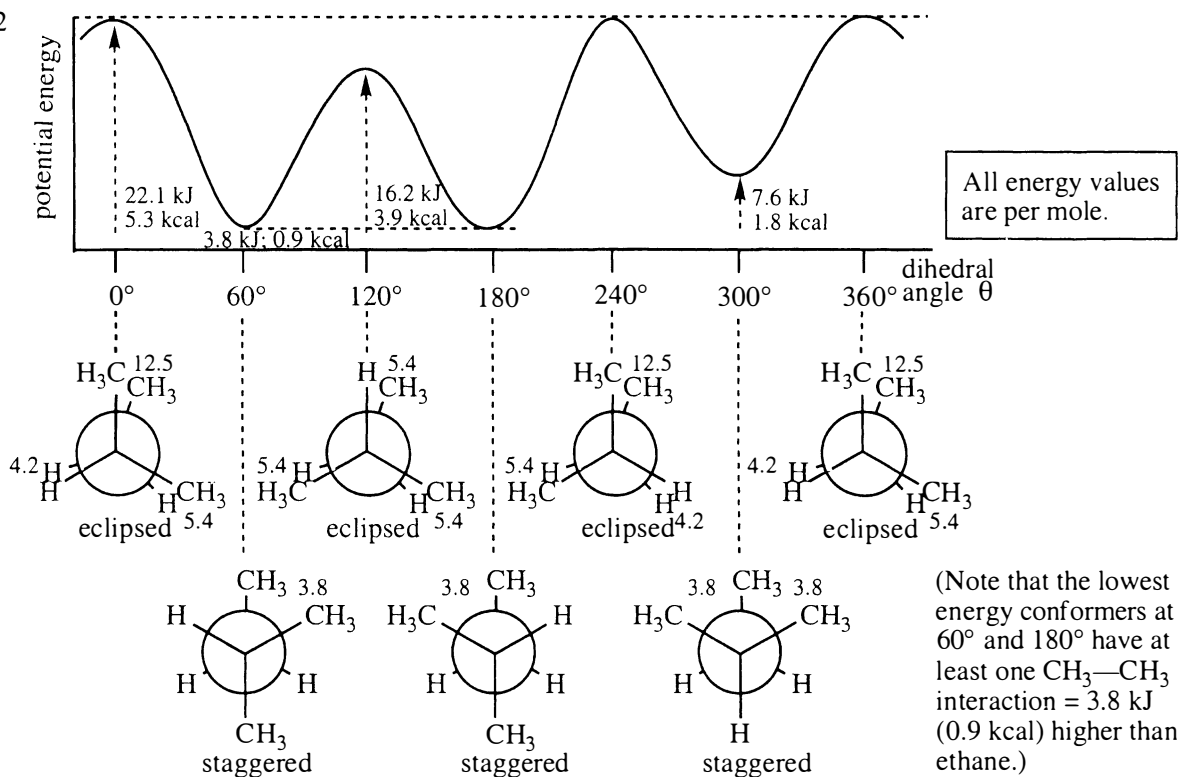
(a) (lowest m.p.) hexane < octane < decane (highest m.p.) —molecular weight

(b) octane < $CH_3CH_2C(CH_3)_2CH_2CH_2CH_3 < (CH_3)_3C-C(CH_3)_3$ —branching
(lowest m.p.) (highest m.p.)

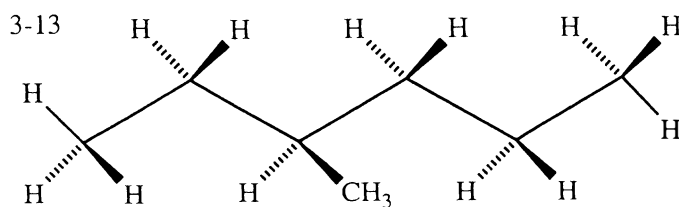
3-11



3-12



Relative energies on the graph above were calculated using these values from the text: 3.8 kJ/mole (0.9 kcal/mole) for a CH₃—CH₃ gauche (staggered) interaction; 4.2 kJ/mole (1.0 kcal/mole) for a H—H eclipsed interaction; 5.4 kJ/mole (1.3 kcal/mole) for a H—CH₃ eclipsed interaction; 12.5 kJ/mole (3.0 kcal/mole) for a CH₃—CH₃ eclipsed interaction. These values in kJ/mole are noted on each structure and are summed to give the energy value on the graph. Slight variation between this graph and the one in the text are due to rounding.



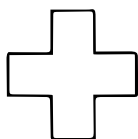
all bonds are staggered

bold bonds are coming toward the reader from the plane of the paper
 dashed bonds are coming toward the reader from the plane of the paper

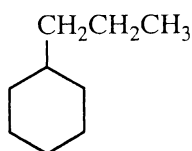
3-14

- (a) 3-*sec*-butyl-1,1-dimethylcyclopentane (the 5-membered ring gives the base name)
 (b) 3-cyclopropyl-1,1-dimethylcyclohexane (the 6-membered ring gives the base name)
 (c) 4-cyclobutylnonane (the chain is longer than the ring)

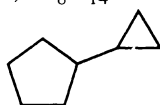
3-15 (a) $C_{12}H_{24}$



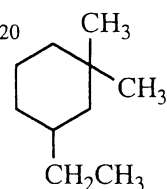
(b) C_9H_{18}



(c) C_8H_{14}

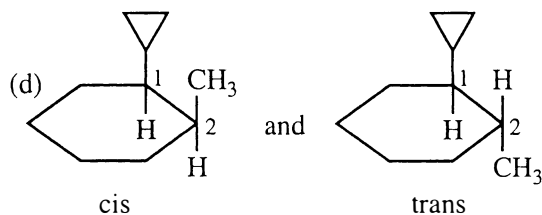
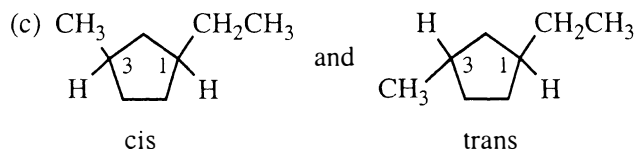
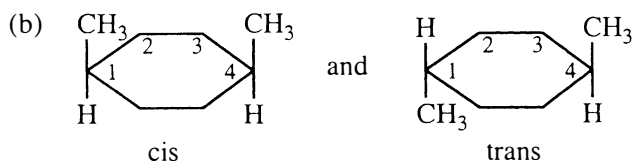


(d) $C_{10}H_{20}$



3-16

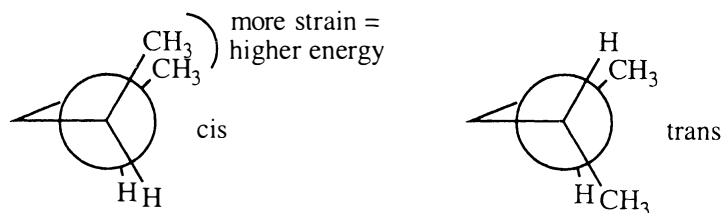
- (a) no cis-trans isomerism possible



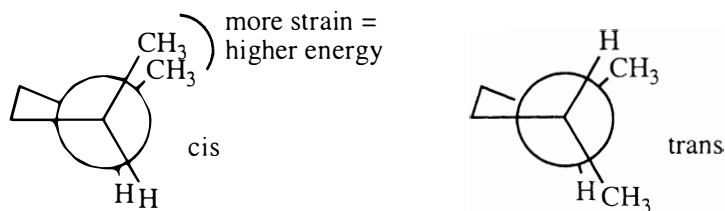
3-17 In (a) and (b), numbering of the ring is determined by the first group *alphabetically* being assigned to ring carbon 1.

- (a) *cis*-1-methyl-3-propylcyclobutane ("m" comes before "p"—practice that alphabet!)
 (b) *trans*-1-*t*-butyl-3-ethylcyclohexane (the prefixes *t*, *s*, and *n* are ignored in assigning alphabetical priority)
 (c) *trans*-1,2-dimethylcyclopropane (either carbon with a CH_3 could be carbon-1; the same name results)

3-18 Combustion of the *cis* isomer gives off more energy, so *cis*-1,2-dimethylcyclopropane must start at a higher energy than the *trans* isomer. The Newman projection of the *cis* isomer shows the two methyls are eclipsed with each other; in the *trans* isomer, the methyls are still eclipsed, but with hydrogens, not each other—a lower energy.



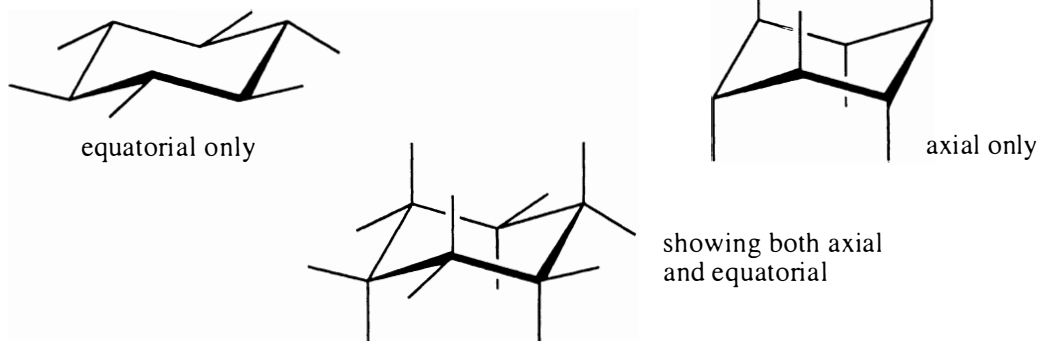
3-19 *trans*-1,2-Dimethylcyclobutane is more stable than *cis* because the two methyls can be farther apart when *trans*, as shown in the Newman projections.



In the 1,3-dimethylcyclobutanes, however, the *cis* allows the methyls to be farther from other atoms and therefore more stable than the *trans*.



3-20

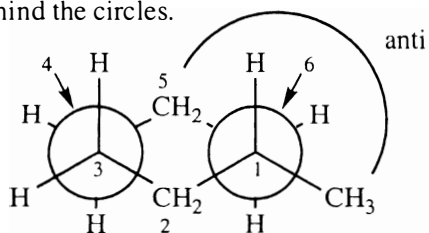


3-21 The abbreviation for a methyl group, CH_3 , is "Me". Ethyl is "Et", propyl is "Pr", and butyl is "Bu".

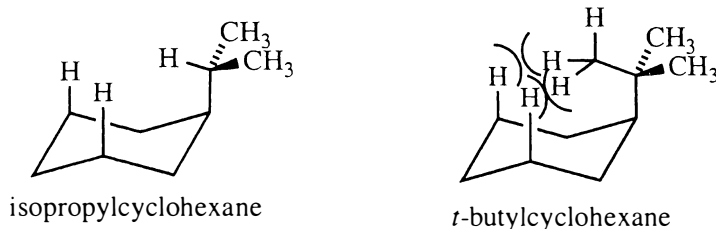


Note that axial groups alternate up and down around the ring.

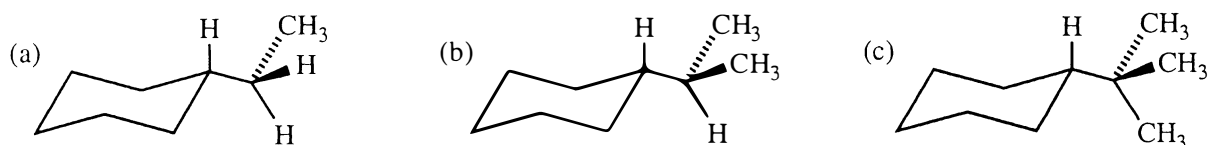
3-22 Carbons 4 and 6 are behind the circles.



3-23 The isopropyl group can rotate so that its hydrogen is near the axial hydrogens on carbons 3 and 5, similar to a methyl group's hydrogen, and therefore similar to a methyl group in energy. The *t*-butyl group, however, must point a methyl group toward the hydrogens on carbons 3 and 5, giving severe diaxial interactions, causing the energy of this conformer to jump dramatically.

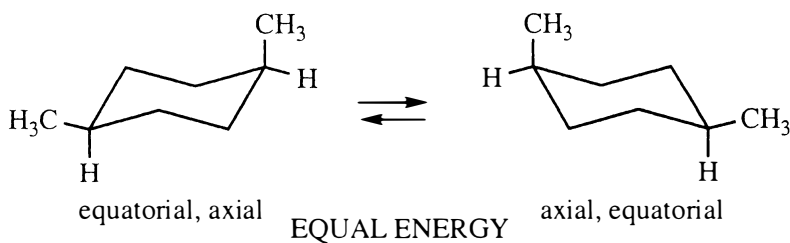


3-24 The most stable conformers have substituents equatorial.

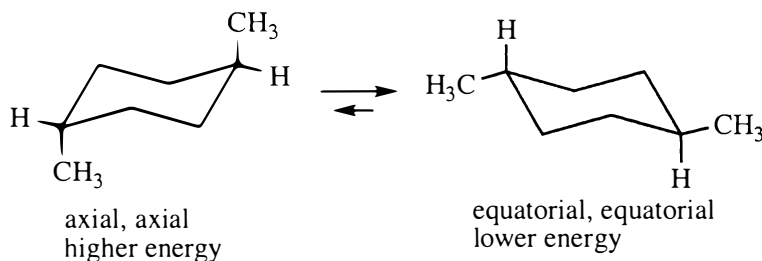


3-25

(a) cis



(b) trans

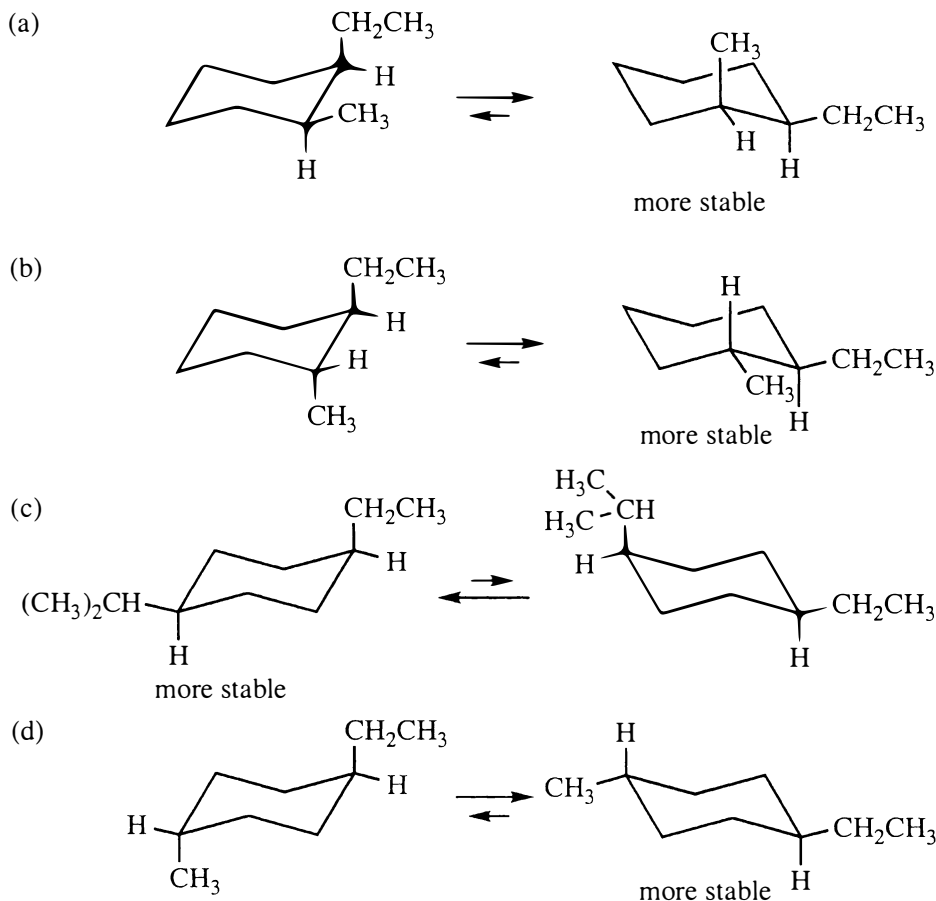


(c) The trans isomer is more stable because BOTH substituents can be in the preferred equatorial positions.

3-26

<i>Positions</i>	<i>cis</i>	<i>trans</i>
1,2	(e,a) or (a,e)	(e,e) or (a,a)
1,3	(e,e) or (a,a)	(e,a) or (a,e)
1,4	(e,a) or (a,e)	(e,e) or (a,a)

3-27 The more stable conformer places the larger group equatorial.

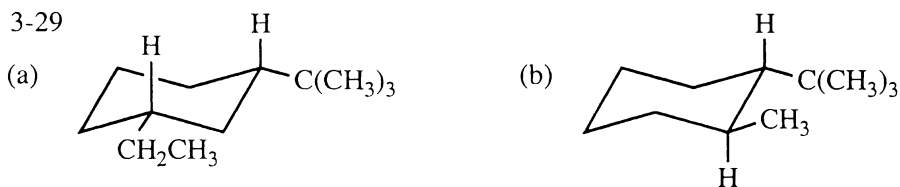


3-28 The key to determining cis and trans around a cyclohexane ring is to see whether a substituent group is "up" or "down" *relative to the H at the same carbon*. Two "up" groups or two "down" groups will be cis; one "up" and one "down" will be trans. This works independent of the conformation the molecule is in!

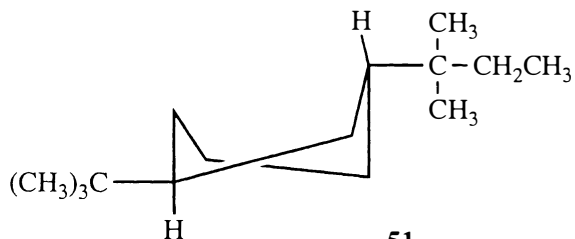
- (a) *cis*-1,3-dimethylcyclohexane
 (b) *cis*-1,4-dimethylcyclohexane
 (c) *trans*-1,2-dimethylcyclohexane

- (d) *cis*-1,3-dimethylcyclohexane
 (e) *cis*-1,3-dimethylcyclohexane
 (f) *trans*-1,4-dimethylcyclohexane

3-29



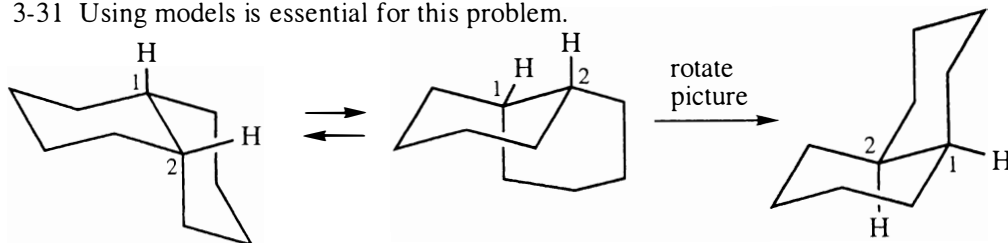
(c) Bulky substituents like *t*-butyl adopt equatorial rather than axial positions, even if that means altering the conformation of the ring. The twist boat conformation allows both bulky substituents to be "equatorial".



3-30 The nomenclature of bicyclic alkanes is summarized in Appendix 1.

(a) bicyclo[3.1.0]hexane (b) bicyclo[3.3.1]nonane (c) bicyclo[2.2.2]octane (d) bicyclo[3.1.1]heptane

3-31 Using models is essential for this problem.



from text Figure 3-29

3-32 Please refer to solution 1-20, page 12 of this Solutions Manual.

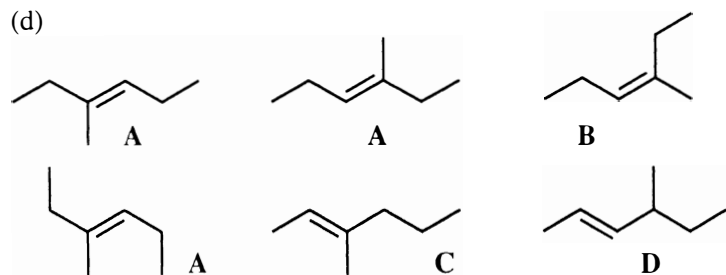
3-33

(a) The third structure is 2-methylpropane (isobutane). The other four structures are all *n*-butane. Remember that a compound's identity is determined by how the atoms are connected, not by the position of the atoms when a structure is drawn on a page.

(b) The two structures at the top-left and bottom-left are both *cis*-2-butene. The two structures at the top-center and bottom-center are both 1-butene. The unique structure at the upper right is *trans*-2-butene. The unique structure at the lower right is 2-methylpropene.

(c) The first two structures are both *cis*-1,2-dimethylcyclopentane. The next two structures are both *trans*-1,2-dimethylcyclopentane. The last structure is different from all the others, *cis*-1,3-dimethylcyclopentane.

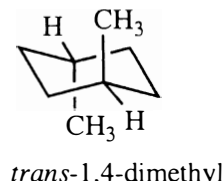
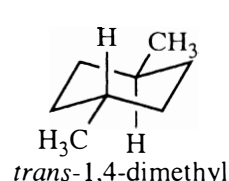
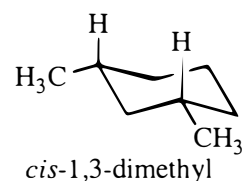
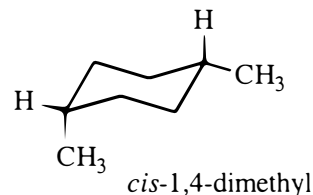
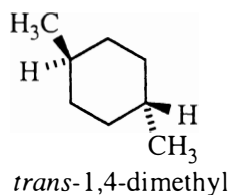
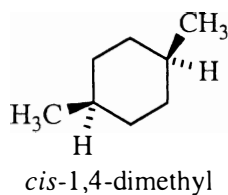
(d)



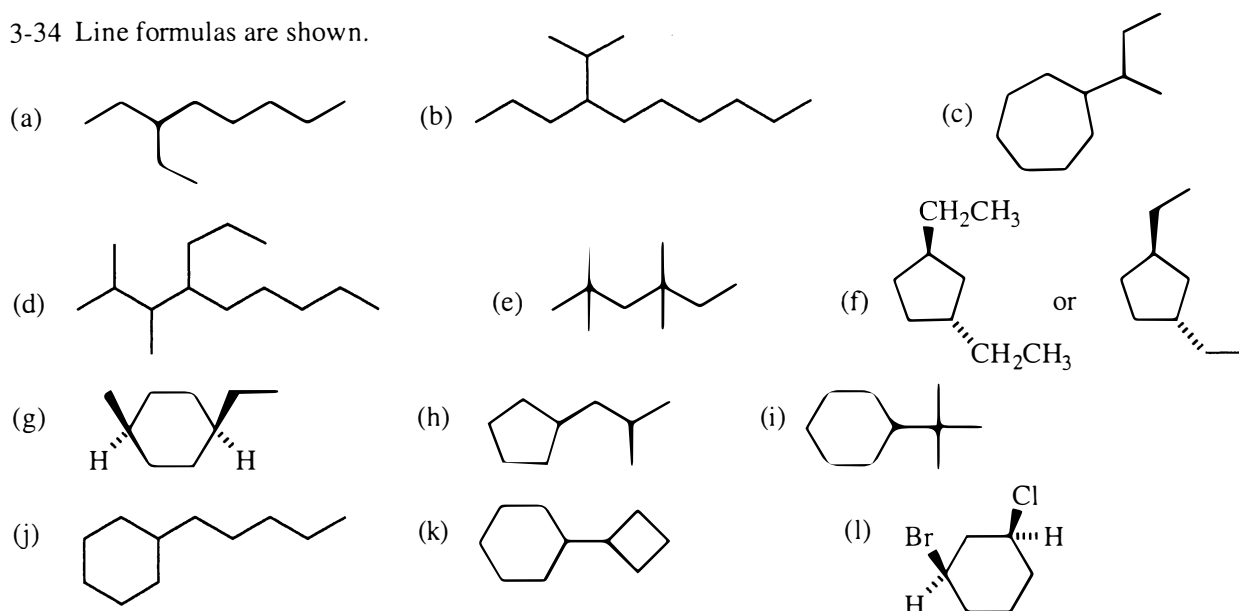
Analysis of the structures shows that some double bonds begin at carbon-2 and some at carbon-3 of the longest chain.

The three structures labeled **A** are the same, with the double bond *trans*; **B** is a geometric isomer (*cis*) of **A**. **C** and **D** are constitutional isomers of the others.

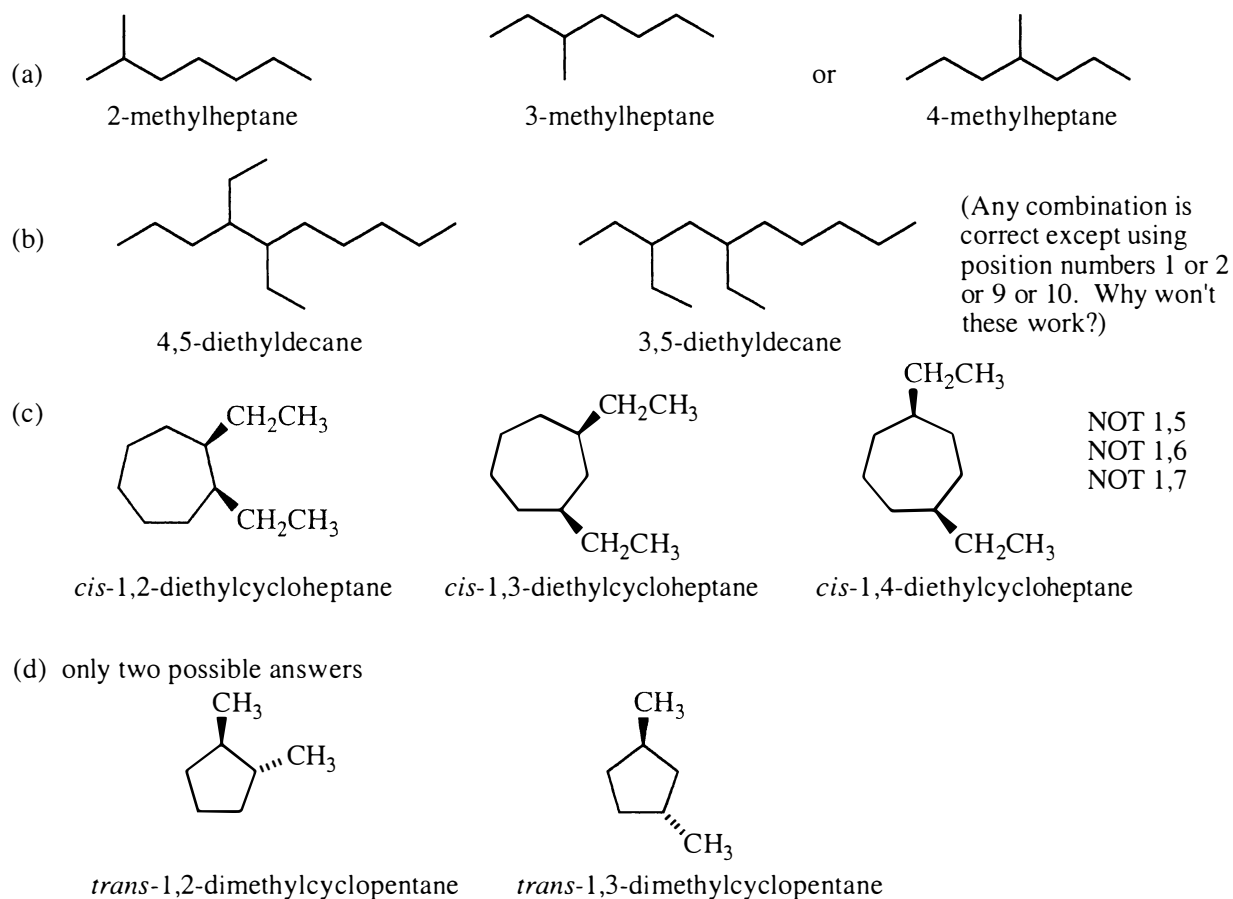
(e) Naming the structures shows that three of the structures are *trans*-1,4-dimethylcyclohexane, two are the *cis* isomer, and one is *cis*-1,3-dimethylcyclohexane. Although a structure may be shown in two different conformations, it still represents only one compound.



3-34 Line formulas are shown.

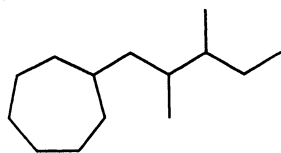


3-35 There are many possible answers to each of these problems. The ones shown here are examples of correct answers. Your answers may be different AND correct. Check your answers in your study group.

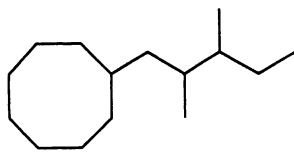


3-35 continued

(e)



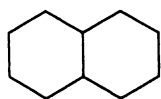
(2,3-dimethylpentyl)cycloheptane



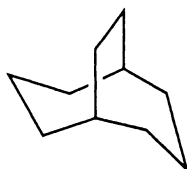
(2,3-dimethylpentyl)cyclooctane

Other ring sizes are possible, although they must have 6 or more carbons to be longer than the 5 carbons of the substituent chain.

(f)



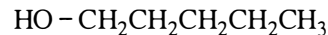
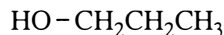
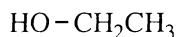
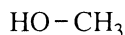
bicyclo[4.4.0]decane



bicyclo[3.3.2]decane

Any combination where the number of carbons in the bridges sums to 8 will work. (Two carbons are the bridgehead carbons.)

3-36



3-37

(a) 3-ethyl-2,2,6-trimethylheptane

(b) 3-ethyl-2,6,7-trimethyloctane

(c) 3,7-diethyl-2,2,8-trimethyldecane

(d) 2-ethyl-1,1-dimethylcyclobutane

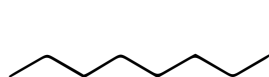
(e) bicyclo[4.1.0]heptane

(f) *cis*-1-ethyl-3-propylcyclopentane

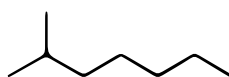
(g) (1,1-diethylpropyl)cyclohexane

(h) *cis*-1-ethyl-4-isopropylcyclodecane

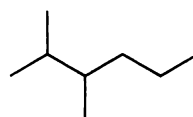
3-38 There are eighteen isomers of C_8H_{18} . Here are eight of them. Yours may be different from the ones shown. An easy way to compare is to name yours and see if the names match.



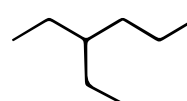
n-octane



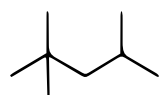
2-methylheptane



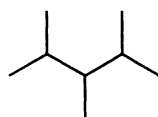
2,3-dimethylhexane



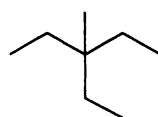
3-ethylhexane



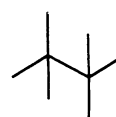
2,2,4-trimethylpentane



2,3,4-trimethylpentane



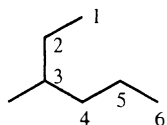
3-ethyl-3-methylpentane



2,2,3,3-tetramethylbutane

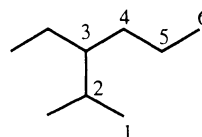
3-39

(a)



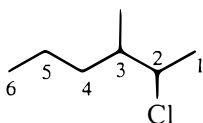
correct name: 3-methylhexane
(longer chain)

(b)



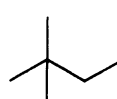
correct name: 3-ethyl-2-methylhexane
(more branching with this numbering)

(c)



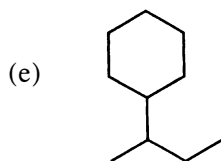
correct name: 2-chloro-3-methylhexane
(begin numbering at end closest to substituent)

(d)

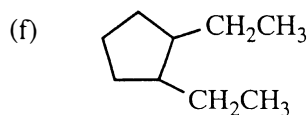


correct name: 2,2-dimethylbutane (include
a position number for each substituent,
regardless of redundancies)

3-39 continued



correct name: *sec*-butylcyclohexane or
(1-methylpropyl)cyclohexane
(the longer chain or ring is the base name)



correct name: 1,2-diethylcyclopentane
(position numbers are the lowest possible)

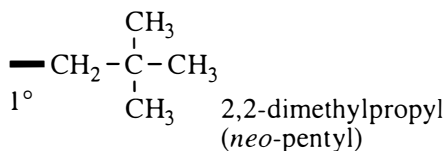
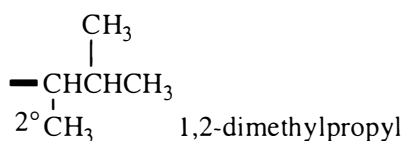
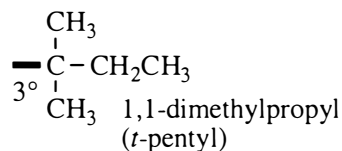
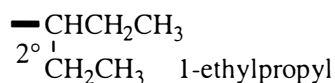
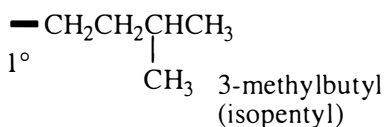
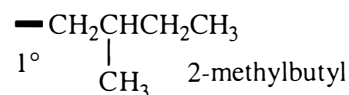
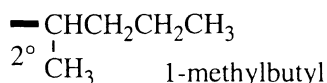
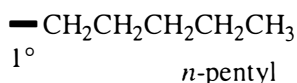
3-40

(a) *n*-Octane has a higher boiling point than 2,2,3-trimethylpentane because linear molecules boil higher than branched molecules of the same molecular weight (increased van der Waals interaction).

(b) 2-Methylnonane has a higher boiling point than *n*-heptane because it has a significantly higher molecular weight than *n*-heptane.

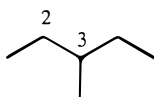
(c) *n*-Nonane boils higher than 2,2,5-trimethylhexane for the same reason as in (a).

3-41 The point of attachment is shown by the bold bond at the left of each structure.

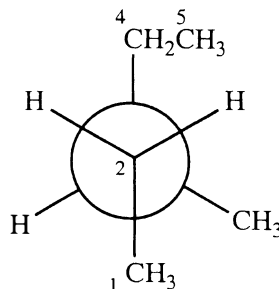


3-42 In each case, put the largest groups on adjacent carbons in anti positions to make the most stable conformations.

(a) 3-methylpentane



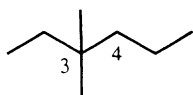
C-2 is the front carbon with H, H, and CH₃
C-3 is the back carbon with H, CH₃, and CH₂CH₃



carbon-3 cannot be seen;
it is behind carbon-2

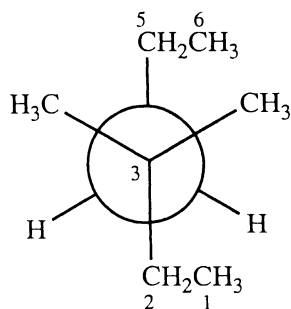
3-42 continued

(b) 3,3-dimethylhexane



C-3 is the front carbon with CH_3 , CH_3 , and CH_2CH_3

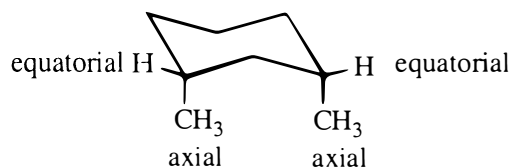
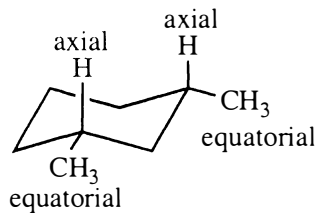
C-4 is the back carbon with H, H, and CH_2CH_3



carbon-4 cannot be seen;
it is behind carbon-3

3-43

(a)



(b) more stable
(lower energy)

less stable
(higher energy)

(c) From Section 3-14 of the text, each gauche interaction raises the energy 3.8 kJ/mole (0.9 kcal/mole), and each axial methyl has two gauche interactions, so the energy is:

2 methyls $\times$ 2 interactions per methyl $\times$ 3.8 kJ/mole per interaction = 15.2 kJ/mole (3.6 kcal/mole)

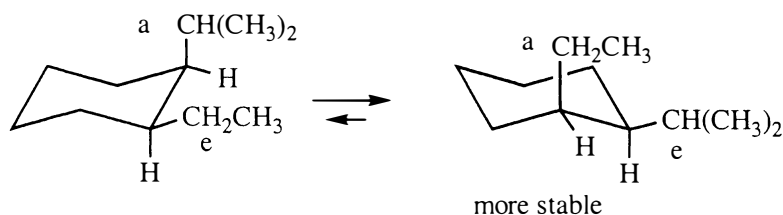
(d) The steric strain from the 1,3-diaxial interaction of the methyls must be the difference between the total energy and the energy due to gauche interactions:

$$23 \text{ kJ/mole} - 15.2 \text{ kJ/mole} = 7.8 \text{ kJ/mole}$$

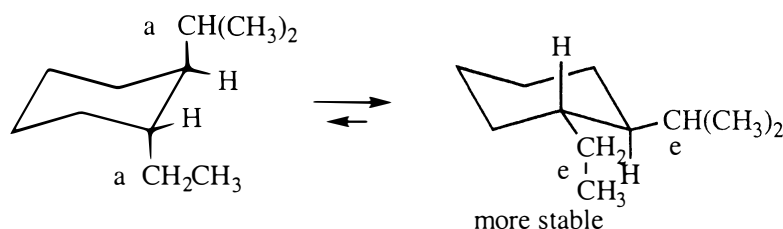
$$(5.4 \text{ kcal/mole} - 3.6 \text{ kcal/mole} = 1.8 \text{ kcal/mole})$$

3-44 The more stable conformer places the larger group equatorial.

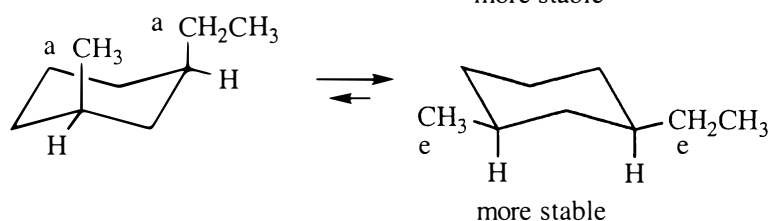
(a)



(b)

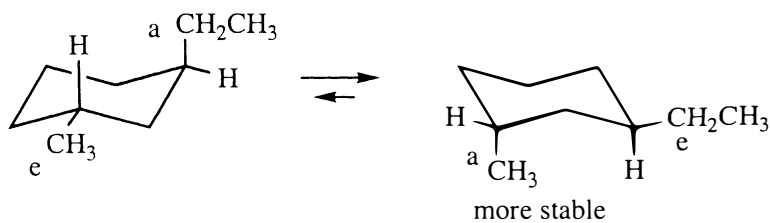


(c)

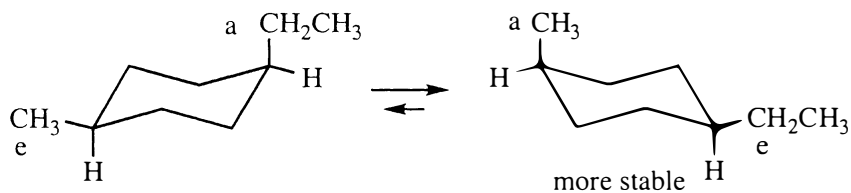


3-44 continued

(d)

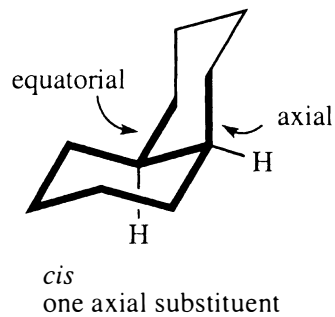
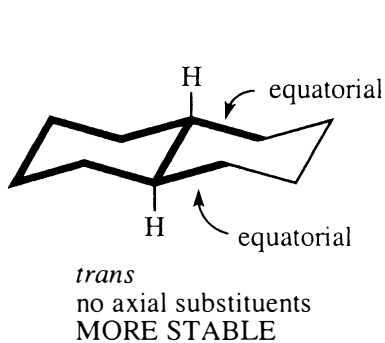


(e)

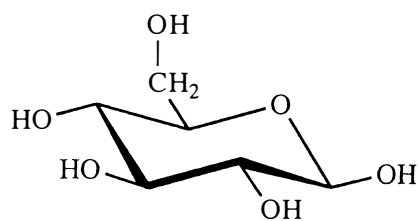
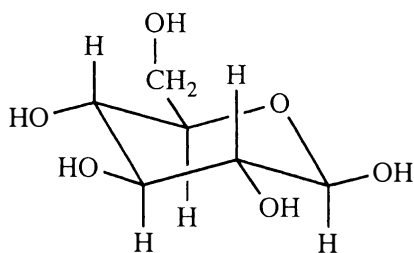


3-45 (Using models is essential to this problem.)

In both *cis*- and *trans*-decalin, the cyclohexane rings can be in chair conformations. The relative energies will depend on the number of axial substituents.



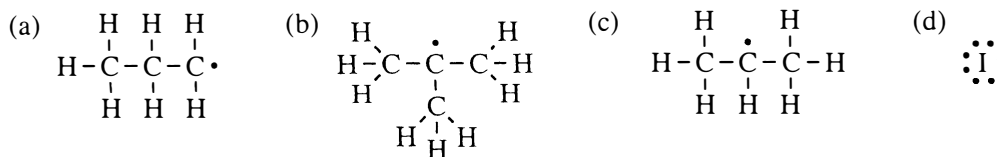
3-46 chair form of glucose—all substituents equatorial



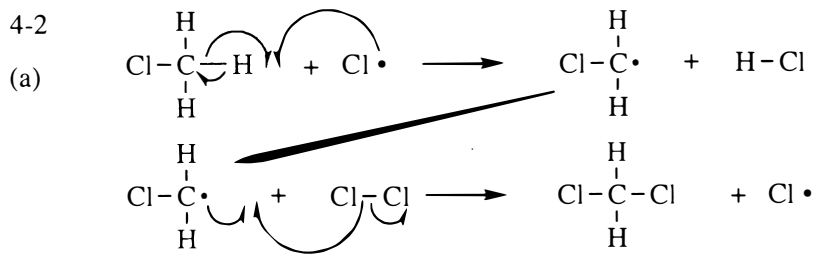
(without ring H's shown)

CHAPTER 4—THE STUDY OF CHEMICAL REACTIONS

4-1



4-2



(b) Free-radical halogenation substitutes a halogen atom for a hydrogen. Even if a molecule has only one type of hydrogen, substitution of the first of these hydrogens forms a new compound. Any remaining hydrogens in this product can compete with the initial reactant for the available halogen. Thus, chlorination of methane, CH_4 , produces all possible substitution products: CH_3Cl , CH_2Cl_2 , CHCl_3 , and CCl_4 .

If a molecule has different types of hydrogens, the reaction can generate a mixture of the possible substitution products.

(c) Production of CCl_4 or CH_3Cl can be controlled by altering the ratio of CH_4 to Cl_2 . To produce CCl_4 , use an excess of Cl_2 and let the reaction proceed until all C—H bonds have been replaced with C—Cl bonds. Producing CH_3Cl is more challenging because the reaction tends to proceed past the first substitution. By using a very large excess of CH_4 to Cl_2 , perhaps 100 to 1 or even more, a chlorine atom is more likely to find a CH_4 molecule than it is to find a CH_3Cl , so only a small amount of CH_4 is transformed to CH_3Cl by the time the Cl_2 runs out, with almost no CH_2Cl_2 being produced.

4-3

(a) This mechanism requires that one photon of light be added for each CH_3Cl generated, a quantum yield of 1. The actual quantum yield is several hundred or thousand. The high quantum yield suggests a chain reaction, but this mechanism is not a chain; it has no propagation steps.

(b) This mechanism conflicts with at least two experimental observations. First, the energy of light required to break a H—CH_3 bond is 435 kJ/mole (104 kcal/mole, from Table 4-2); the energy of light determined by experiment to initiate the reaction is only 251 kJ/mole of photons (60 kcal/mole of photons), much less than the energy needed to break this H—C bond. Second, as in (a), each CH_3Cl produced would require one photon of light, a quantum yield of 1, instead of the actual number of several hundred or thousand. As in (a), there is no provision for a chain process, since all the radicals generated are also consumed in the mechanism.

4-4

(a) The twelve hydrogens of cyclohexane are all on equivalent 2° carbons. Replacement of any one of the twelve will lead to the same product, chlorocyclohexane. *n*-Hexane, however, has hydrogens in three different positions: on carbon-1 (equivalent to carbon-6), carbon-2 (equivalent to carbon-5), and carbon-3 (equivalent to carbon-4). Monochlorination of *n*-hexane will produce a mixture of all three possible isomers: 1-, 2-, and 3-chlorohexane.

4-4 continued

(b) The best conversion of cyclohexane to chlorocyclohexane would require the ratio of cyclohexane/chlorine to be a large number. If the ratio were small, as the concentration of chlorocyclohexane increased during the reaction, chlorine would begin to substitute for a second hydrogen of chlorocyclohexane, generating unwanted products. The goal is to have chlorine attack a molecule of cyclohexane before it ever encounters a molecule of chlorocyclohexane, so the concentration of cyclohexane should be kept high.

4-5

$$\begin{aligned} (a) \quad K_{eq} &= e^{-\Delta G^\circ/RT} = e^{-2.1 \text{ kJ/mole} = -2100 \text{ J/mole}} & K = \text{degrees kelvin} \\ &= e^{-(-2100 \text{ J/mole})/((8.314 \text{ J/K-mole}) \cdot (298 \text{ K}))} \\ &= e^{2100 / 2478} = e^{0.847} = \boxed{2.3} \end{aligned}$$

$$(b) \quad K_{eq} = 2.3 = \frac{[\text{CH}_3\text{SH}] [\text{HBr}]}{[\text{CH}_3\text{Br}] [\text{H}_2\text{S}]}$$

	$[\text{CH}_3\text{Br}]$	$[\text{H}_2\text{S}]$	$[\text{CH}_3\text{SH}]$	$[\text{HBr}]$
initial concentrations:	1	1	0	0
final concentrations	$1 - x$	$1 - x$	x	x

$$K_{eq} = 2.3 = \frac{x \cdot x}{(1-x)(1-x)} = \frac{x^2}{1 - 2x + x^2} \implies x^2 = 2.3 x^2 - 4.6 x + 2.3$$

$$0 = 1.3 x^2 - 4.6 x + 2.3 \implies x = 0.60, \quad 1 - x = 0.40$$

(using quadratic equation)

$$\boxed{[\text{CH}_3\text{SH}] = [\text{HBr}] = 0.60 \text{ M}; [\text{CH}_3\text{Br}] = [\text{H}_2\text{S}] = 0.40 \text{ M}}$$

4-6 $2 \text{ acetone} \rightleftharpoons \text{diacetone}$

Assume that the initial concentration of acetone is 1 molar, and 5% of the acetone is converted to diacetone. NOTE THE MOLE RATIO.

	[acetone]	[diacetone]
initial concentrations:	1 M	0
final concentrations:	0.95 M	0.025 M

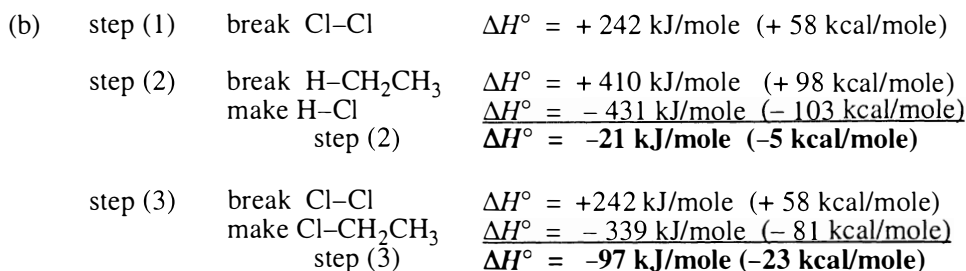
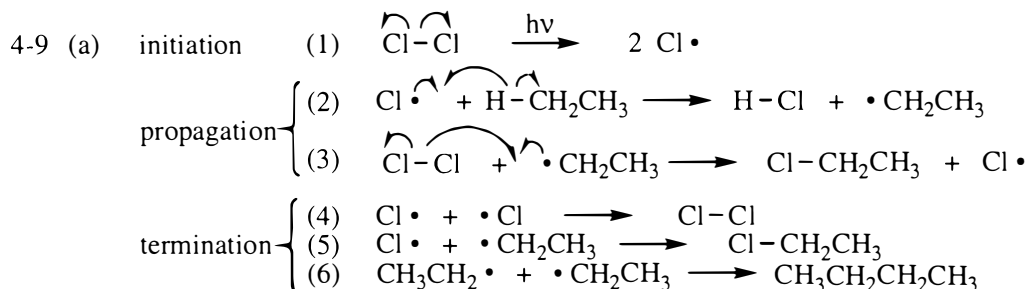
$$K_{eq} = \frac{[\text{diacetone}]}{[\text{acetone}]^2} = \frac{0.025}{(0.95)^2} = \boxed{0.028}$$

$$\begin{aligned} \Delta G^\circ &= -2.303 RT \log_{10} K_{eq} = -2.303 ((8.314 \text{ J/K-mole}) \cdot (298\text{K})) \cdot \log(0.028) \\ &= \boxed{+ 8.9 \text{ kJ/mole} \quad (+ 2.1 \text{ kcal/mole})} \end{aligned}$$

4-7 ΔS° will be negative since two molecules are combined into one, a loss of freedom of motion. Since ΔS° is negative, $-T\Delta S^\circ$ is positive; but ΔG° is a large negative number since the reaction goes to completion. Therefore, ΔH° must also be a large negative number, necessarily larger in absolute value than ΔG° . We can explain this by formation of two strong C-H bonds (410 kJ/mole each) after breaking a strong H-H bond (435 kJ/mole) and a WEAKER C=C pi bond.

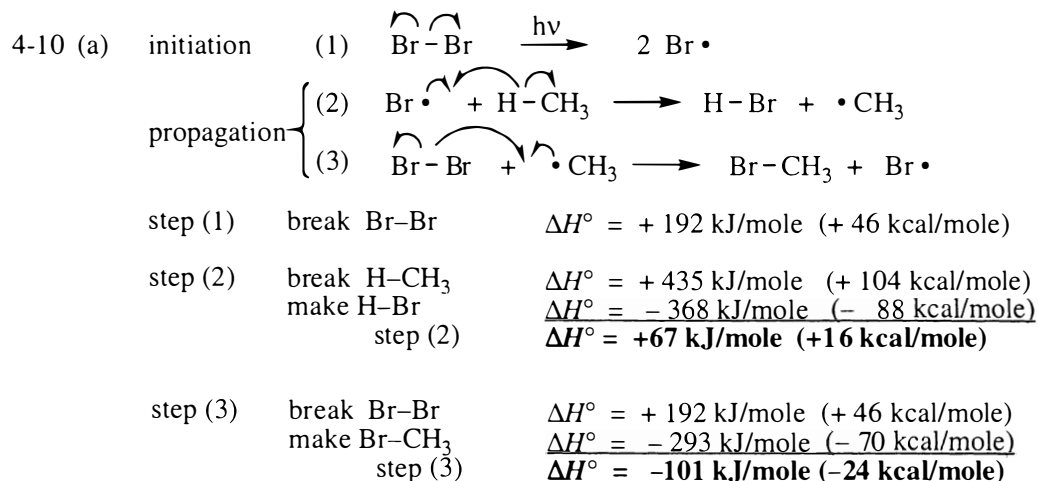
4-8

- (a) ΔS° is positive—one molecule became two smaller molecules with greater freedom of motion
 (b) ΔS° is negative—two smaller molecules combined into one larger molecule with less freedom of motion
 (c) ΔS° cannot be predicted since the number of molecules in reactants and products is the same



(c) ΔH° for the reaction is the sum of the ΔH° values of the individual propagation steps:

$$\begin{aligned} -21 \text{ kJ/mole} + -97 \text{ kJ/mole} &= -118 \text{ kJ/mole} \\ (-5 \text{ kcal/mole} + -23 \text{ kcal/mole}) &= -28 \text{ kcal/mole} \end{aligned}$$



(b) ΔH° for the reaction is the sum of the ΔH° values of the individual propagation steps:

$$\begin{aligned} +67 \text{ kJ/mole} + -101 \text{ kJ/mole} &= -34 \text{ kJ/mole} \\ (+16 \text{ kcal/mole} + -24 \text{ kcal/mole}) &= -8 \text{ kcal/mole} \end{aligned}$$

4-11

- (a) first order: the exponent of $[(\text{CH}_3)_3\text{CCl}]$ in the rate law = 1
- (b) zeroth order: $[\text{CH}_3\text{OH}]$ does not appear in the rate law (its exponent is zero)
- (c) first order: the sum of the exponents in the rate law = $1 + 0 = 1$

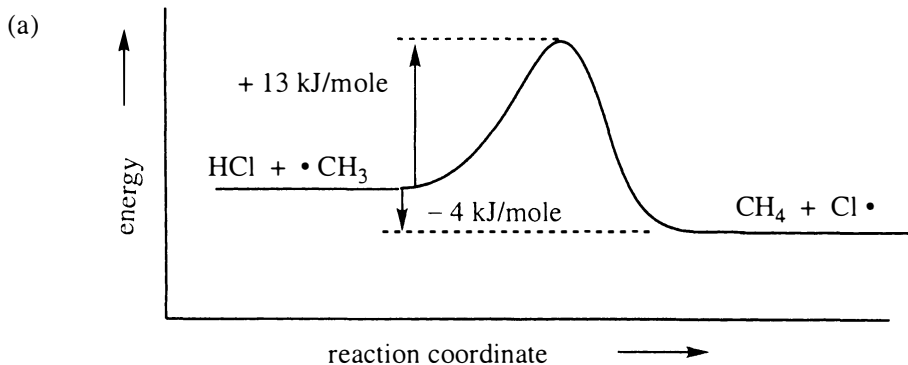
4-12

- (a) first order: the exponent of [cyclohexene] in the rate law = 1
- (b) second order: the exponent of $[\text{Br}_2]$ in the rate law = 2
- (c) third order: the sum of the exponents in the rate law = $1 + 2 = 3$

4-13

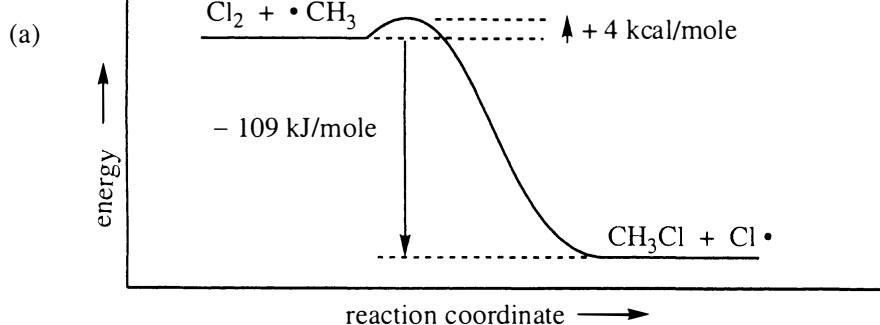
- (a) the reaction rate depends on neither [ethylene] nor [hydrogen], so it is zeroth order in both species. The overall reaction must be zeroth order.
- (b) rate = k_r
- (c) The rate law does not depend on the concentration of the reactants. It must depend, therefore, on the only other chemical present, the catalyst. Apparently, whatever is happening on the surface of the catalyst determines the rate, regardless of the concentrations of the two gases. Increasing the surface area of the catalyst, or simply adding more catalyst, would accelerate the reaction.

4-14

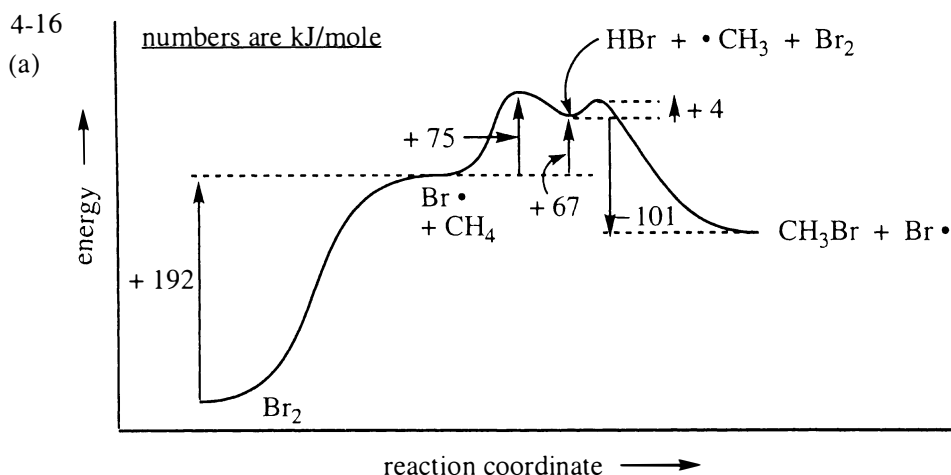


- (b) $E_a = +13 \text{ kJ/mole}$ ($+3 \text{ kcal/mole}$)
- (c) $\Delta H^\circ = -4 \text{ kJ/mole}$ (-1 kcal/mole)

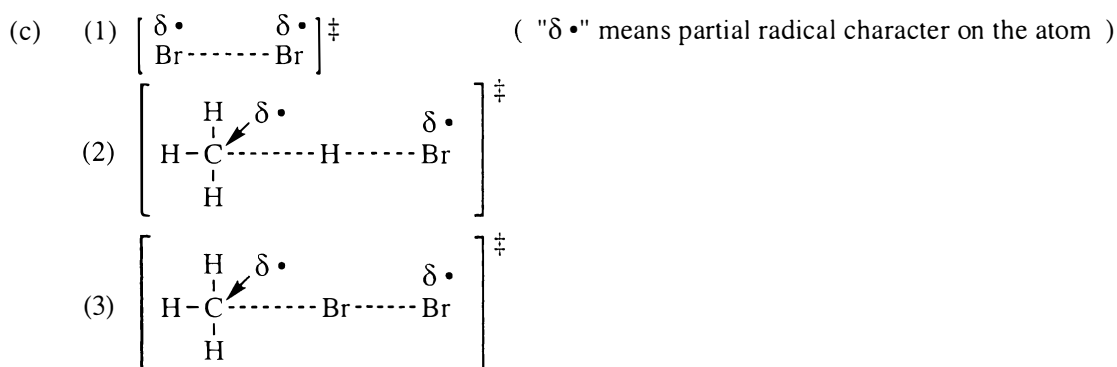
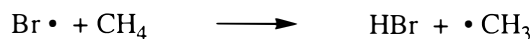
4-15



- (b) reverse: $\text{CH}_3\text{Cl} + \text{Cl}\cdot \longrightarrow \text{Cl}_2 + \cdot\text{CH}_3$
- (c) reverse: $E_a = +109 \text{ kJ/mole} + +4 \text{ kJ/mole} = +113 \text{ kJ/mole}$
 $(+26 \text{ kcal/mole} + +1 \text{ kcal/mole} = +27 \text{ kcal/mole})$



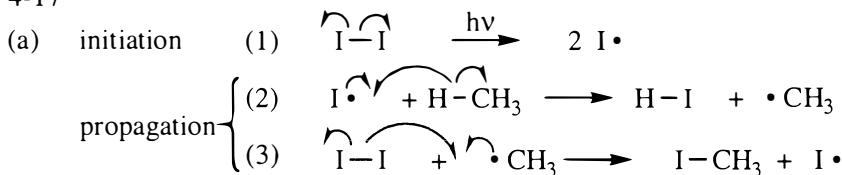
(b) The step leading to the highest energy transition state is rate-limiting. In this mechanism, the first propagation step is rate-limiting:



(d) ΔH° for the reaction is the sum of the ΔH° values of the individual propagation steps (refer to the solution to 4-10 (a) and (b)):

$$\begin{aligned} + 67 \text{ kJ/mole} &+ - 101 \text{ kJ/mole} = - 34 \text{ kJ/mole} \\ (+ 16 \text{ kcal/mole} &+ - 24 \text{ kcal/mole} = - 8 \text{ kcal/mole}) \end{aligned}$$

4-17



step (1) break I-I $\Delta H^\circ = + 151 \text{ kJ/mole}$ (+ 36 kcal/mole)

step (2) break H-CH₃ $\Delta H^\circ = + 435 \text{ kJ/mole}$ (+ 104 kcal/mole)
make H-I $\Delta H^\circ = - 297 \text{ kJ/mole}$ (- 71 kcal/mole)
step (2) $\Delta H^\circ = + 138 \text{ kJ/mole}$ (+ 33 kcal/mole)

step (3) break I-I $\Delta H^\circ = + 151 \text{ kJ/mole}$ (+ 36 kcal/mole)
make I-CH₃ $\Delta H^\circ = - 234 \text{ kJ/mole}$ (- 56 kcal/mole)
step (3) $\Delta H^\circ = - 83 \text{ kJ/mole}$ (- 20 kcal/mole)

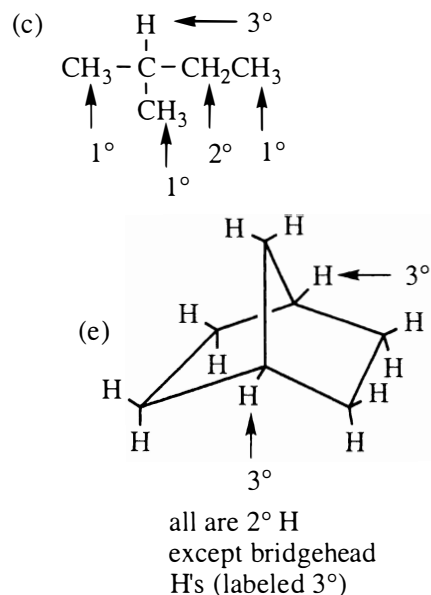
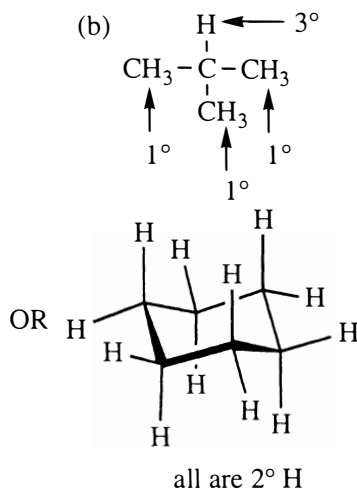
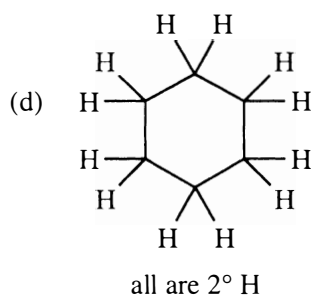
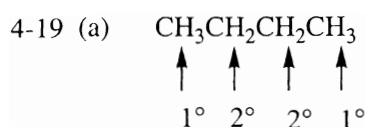
4-17 continued

(b) ΔH° for the reaction is the sum of the ΔH° values of the individual propagation steps:

$$\begin{aligned} &+ 138 \text{ kJ/mole} + - 83 \text{ kJ/mole} = + 55 \text{ kJ/mole} \\ &(+ 33 \text{ kcal/mole} + - 20 \text{ kcal/mole} = + 13 \text{ kcal/mole}) \end{aligned}$$

(c) Iodination of methane is unfavorable for both kinetic and thermodynamic reasons. Kinetically, the rate of the first propagation step must be very slow because it is very endothermic; the activation energy must be at least + 138 kJ/mole. Thermodynamically, the overall reaction is endothermic, so an equilibrium would favor reactants, not products; there is no energy decrease to drive the reaction to products.

4-18 Propane has six primary hydrogens and two secondary hydrogens, a ratio of 3 : 1. If primary and secondary hydrogens were replaced by chlorine at equal rates, the chloropropane isomers would reflect the same 3 : 1 ratio, that is, 75% 1-chloropropane and 25% 2-chloropropane.



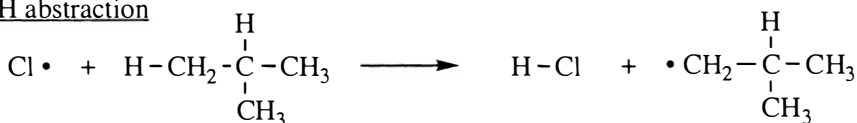
4-20

3° H abstraction



$$\begin{array}{ll} \text{break } 3^\circ \text{ H} - \text{C}(\text{CH}_3)_3 & \Delta H^\circ = + 381 \text{ kJ/mole } (+ 91 \text{ kcal/mole}) \\ \text{make H} - \text{Cl} & \Delta H^\circ = - 431 \text{ kJ/mole } (- 103 \text{ kcal/mole}) \\ \text{overall } 3^\circ \text{ H abstraction} & \Delta H^\circ = - 50 \text{ kJ/mole } (- 12 \text{ kcal/mole}) \end{array}$$

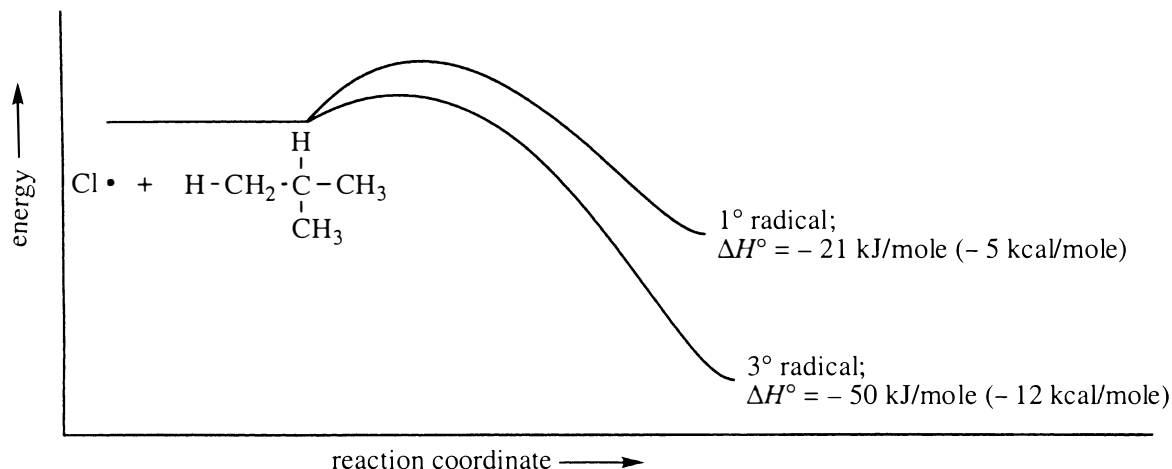
1° H abstraction



$$\begin{array}{ll} \text{break } 1^\circ \text{ H} - \text{CH}_2\text{CH}(\text{CH}_3)_2 & \Delta H^\circ = + 410 \text{ kJ/mole } (+ 98 \text{ kcal/mole}) \\ \text{make H} - \text{Cl} & \Delta H^\circ = - 431 \text{ kJ/mole } (- 103 \text{ kcal/mole}) \\ \text{overall } 1^\circ \text{ H abstraction} & \Delta H^\circ = - 21 \text{ kJ/mole } (- 5 \text{ kcal/mole}) \end{array}$$

(Note: ΔH° for abstraction of a 1° H from both ethane and propane are + 410 kJ/mole (+ 98 kcal/mole). It is reasonable to use this same value for abstraction of the 1° H in isobutane.)

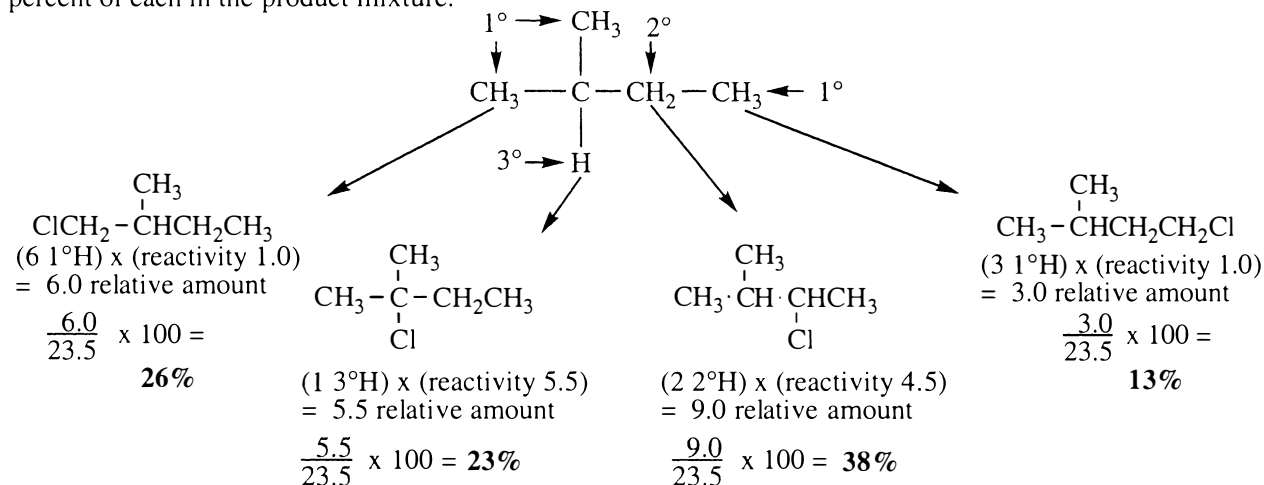
4-20 continued



Since ΔH° for forming the 3° radical is more negative than ΔH° for forming the 1° radical, it is reasonable to infer that the activation energy leading to the 3° radical is lower than the activation energy leading to the 1° radical.

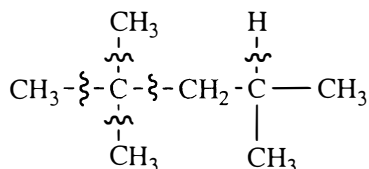
4-21

2-Methylbutane can produce four mono-chloro isomers. To calculate the relative amount of each in the product mixture, multiply the numbers of hydrogens which could lead to that product times the reactivity for that type of hydrogen. Each relative amount divided by the sum of all the amounts will provide the percent of each in the product mixture.



4-22

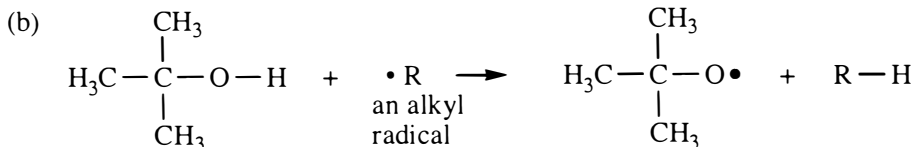
(a) When *n*-heptane is burned, only 1° and 2° radicals can be formed (from either C—H or C—C bond cleavage). These are high energy, unstable radicals which rapidly form other products. When isooctane (2,2,4-trimethylpentane, below) is burned, 3° radicals can be formed from either C—H or C—C bond cleavage. The 3° radicals are lower in energy than 1° or 2° , relatively stable, with lowered reactivity. Slower combustion translates to less "knocking."



isooctane (2,2,4-trimethylpentane)

Any indicated bond cleavage will produce a 3° radical.

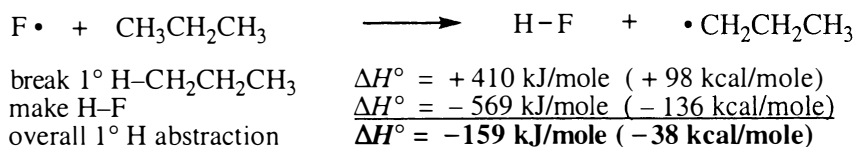
4-22 continued



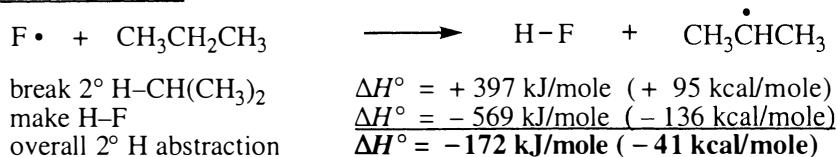
When the alcohol hydrogen is abstracted from *t*-butyl alcohol, a relatively stable *t*-butoxy radical ($(\text{CH}_3)_3\text{C}-\text{O}\bullet$) is produced. This low energy radical is slower to react than alkyl radicals, moderating the reaction and producing less "knocking."

4-23

(a) 1° H abstraction



2° H abstraction

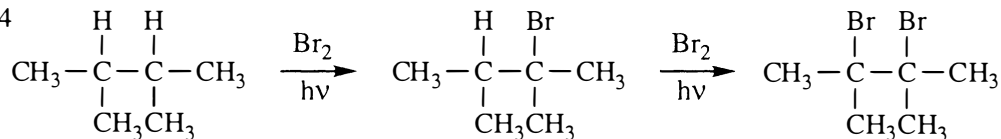


(b) Fluorination is extremely exothermic and is likely to be indiscriminate in which hydrogens are abstracted. (In fact, C—C bonds are also broken during fluorination.)

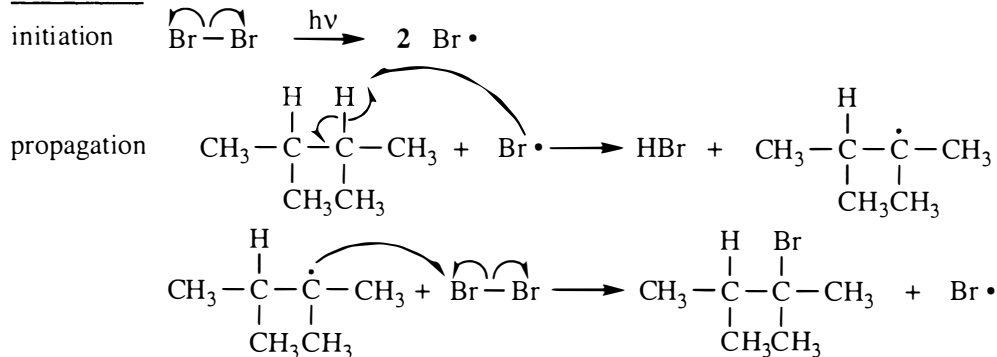
(c) Free radical fluorination is extremely exothermic. In exothermic reactions, the transition states resemble the starting materials more than the products, so while the 1° and 2° radicals differ by about 13 kJ/mole (3 kcal/mole), the transition states will differ by only a tiny amount. For fluorination, then, the rate of abstraction for 1° and 2° hydrogens will be virtually identical. Product ratios will depend on statistical factors only.

Fluorination is difficult to control, but if propane were monofluorinated, the product mixture would reflect the ratio of the types of hydrogens: six 1° H to two 2° H, or 3 : 1 ratio, giving 75% 1-fluoropropane and 25% 2-fluoropropane.

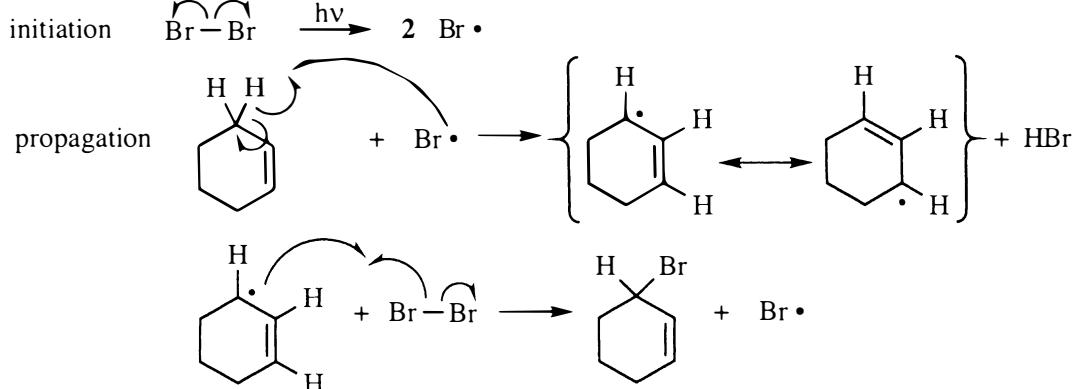
4-24



Mechanism



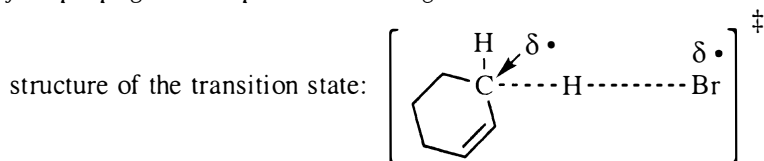
4-25 (a) Mechanism



(b) Energy calculation uses the value for the allylic C—H bond from Table 4-2.

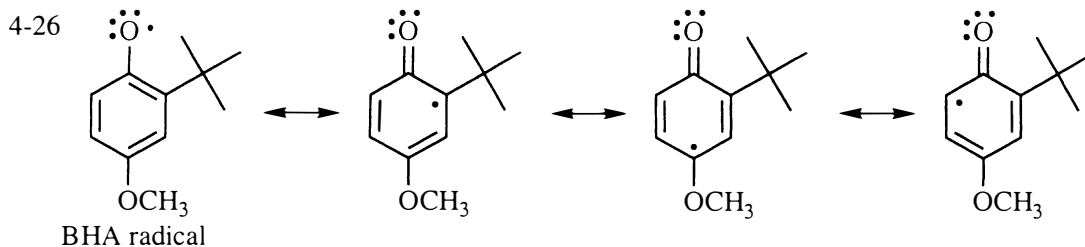
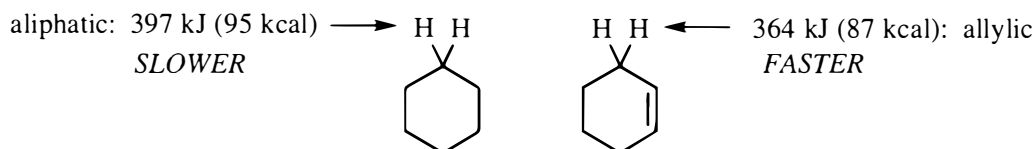
First propagation step	break allylic H—CH[ring]	$\Delta H^\circ = +364 \text{ kJ/mole } (+87 \text{ kcal/mole})$
	make H—Br	$\Delta H^\circ = -368 \text{ kJ/mole } (-88 \text{ kcal/mole})$
	overall allylic H abstraction	$\Delta H^\circ = -4 \text{ kJ/mole } (-1 \text{ kcal/mole})$
Second propagation step	break Br—Br	$\Delta H^\circ = +192 \text{ kJ/mole } (+46 \text{ kcal/mole})$
	make 2° C—Br	$\Delta H^\circ = -285 \text{ kJ/mole } (-68 \text{ kcal/mole})$
	overall C—Br formation	$\Delta H^\circ = -93 \text{ kJ/mole } (-22 \text{ kcal/mole})$

The first propagation step is rate-limiting.

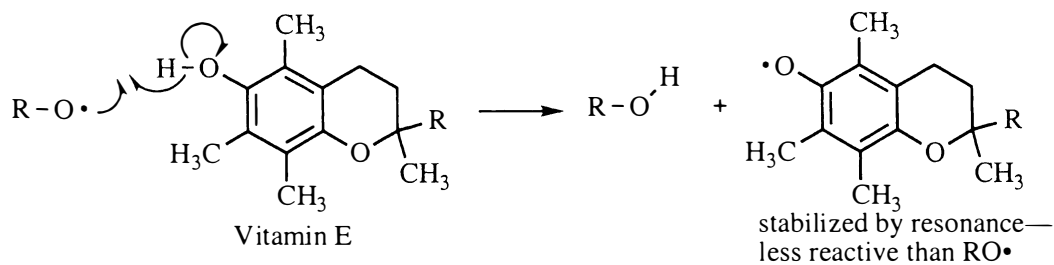


(c) The Hammond postulate tells us that, in an exothermic reaction, the transition state is closer to the reactants in energy and in structure. Since the first propagation step is exothermic (although not by much), the transition state is closer to cyclohexene + bromine radical. This is indicated in the transition state structure by showing the H closer to the C than to the Br.

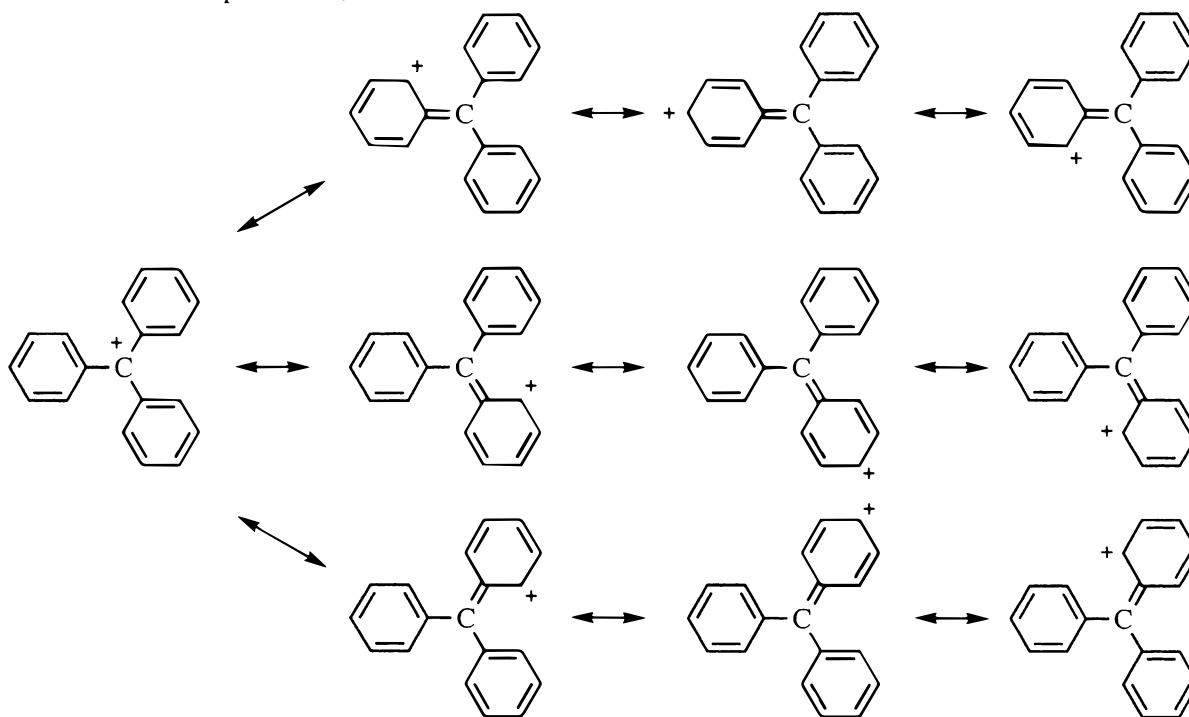
(d) A bromine radical will abstract the hydrogen with the lowest bond dissociation energy at the fastest rate. The allylic hydrogen of cyclohexene is more easily abstracted than a hydrogen of cyclohexane because the radical produced is stabilized by resonance. (Energy values below are per mole.)



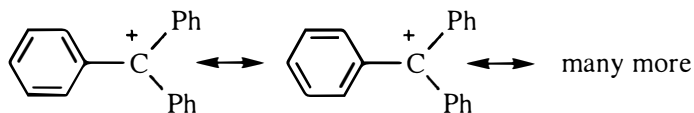
4-27



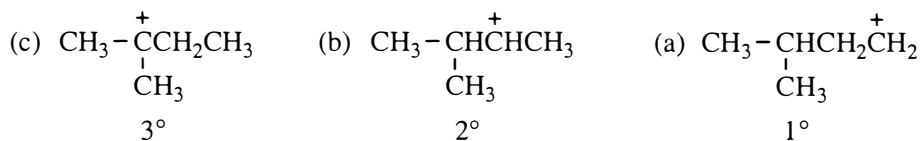
4-28 The triphenylmethyl cation is so stable because of the delocalization of the charge. The more resonance forms a species has, the more stable it will be.



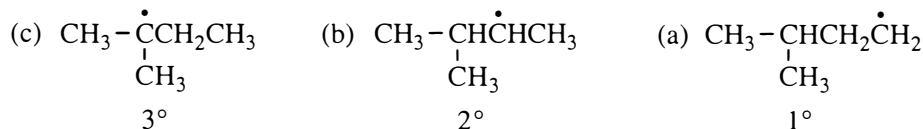
(Note: these resonance forms do not include the simple benzene resonance forms as shown below; they are significant, but repetitive, so for simplicity, they are not drawn here.)



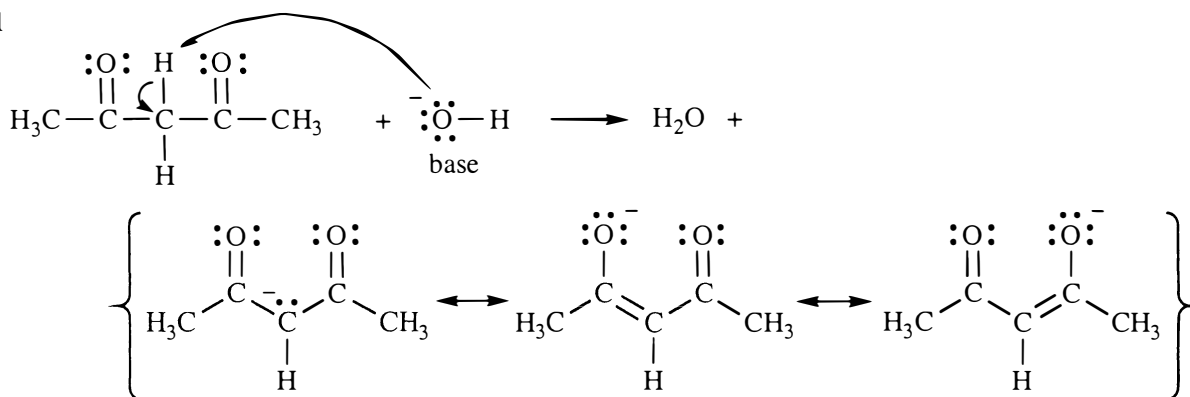
4-29 most stable (c) > (b) > (a) least stable



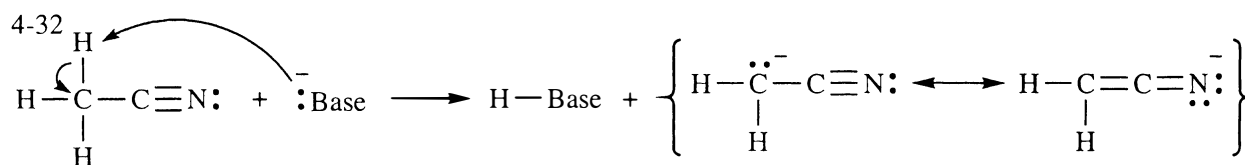
4-30 most stable (c) > (b) > (a) least stable



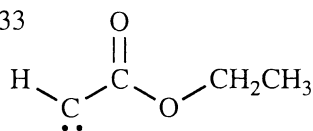
4-31



4-32



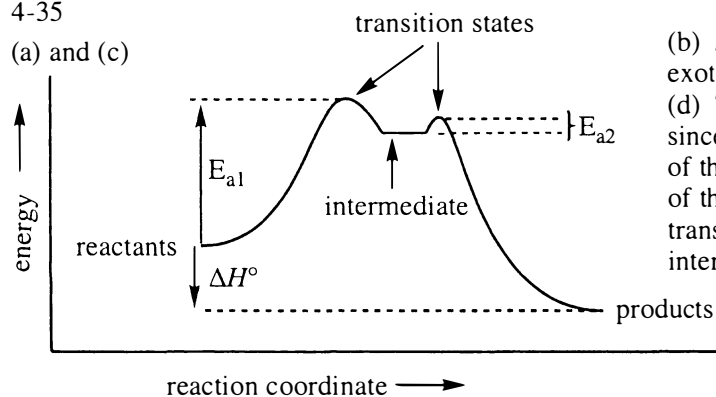
4-33



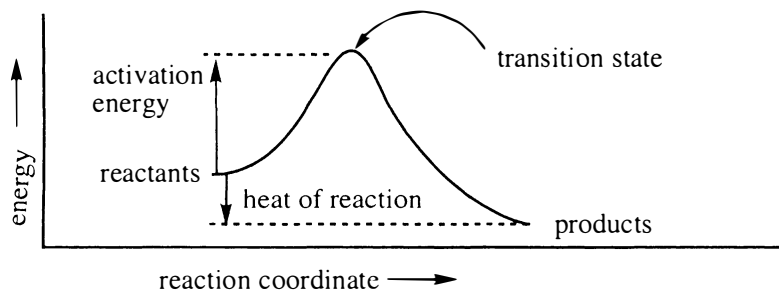
4-34 Please refer to solution 1-20, page 12 of this Solutions Manual.

4-35

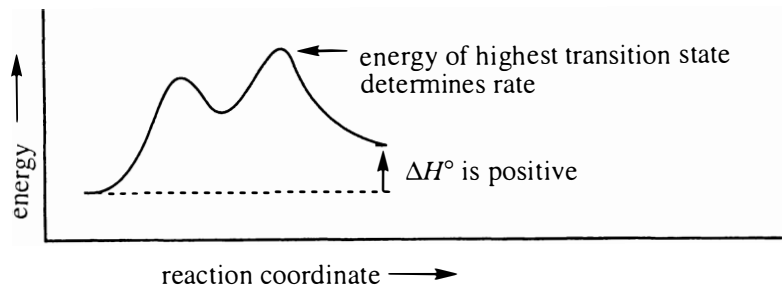
(a) and (c)

(b) ΔH° is negative (decreases), so the reaction is exothermic.(d) The first transition state determines the rate since it is the highest energy point. The *structure* of the first transition state resembles the *structure* of the intermediate since the *energy* of the transition state is closest to the *energy* of the intermediate.

4-36



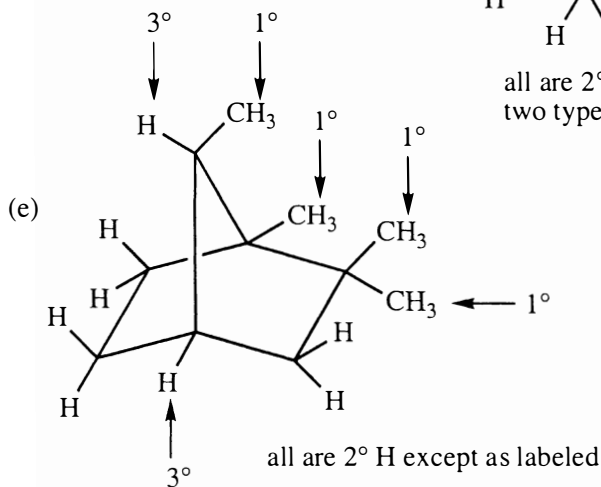
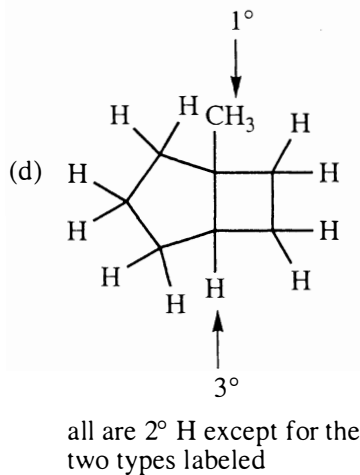
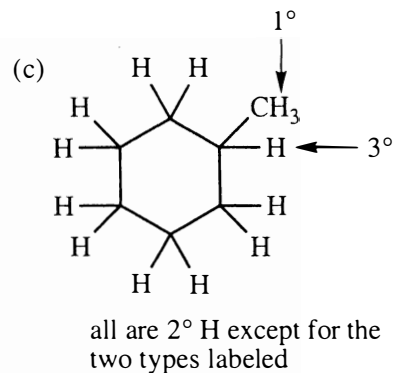
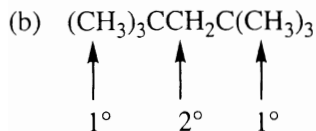
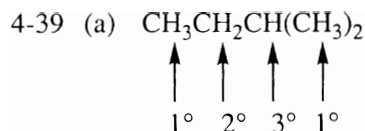
4-37



4-38

The rate law is first order with respect to the concentrations of hydrogen ion and of *t*-butyl alcohol, zeroth order with respect to the concentration of chloride ion, second order overall.

$$\text{rate} = k_r [(\text{CH}_3)_3\text{COH}] [\text{H}^+]$$



4-40

(a) break $\text{H}-\text{CH}_2\text{CH}_3$ and $\text{I}-\text{I}$, make $\text{I}-\text{CH}_2\text{CH}_3$ and $\text{H}-\text{I}$

$$\text{kJ/mole: } (+410 + +151) + (-222 + -297) = +42 \text{ kJ/mole}$$

$$\text{kcal/mole: } (+98 + +36) + (-53 + -71) = +10 \text{ kcal/mole}$$

(b) break $\text{CH}_3\text{CH}_2-\text{Cl}$ and $\text{H}-\text{I}$, make $\text{CH}_3\text{CH}_2-\text{I}$ and $\text{H}-\text{Cl}$

$$\text{kJ/mole: } (+339 + +297) + (-222 + -431) = -17 \text{ kJ/mole}$$

$$\text{kcal/mole: } (+81 + +71) + (-53 + -103) = -4 \text{ kcal/mole}$$

4-40 continued

(c) break $(\text{CH}_3)_3\text{C}-\text{OH}$ and $\text{H}-\text{Cl}$, make $(\text{CH}_3)_3\text{C}-\text{Cl}$ and $\text{H}-\text{OH}$

$\text{kJ/mole: } (+381 + +431) + (-331 + -498) = -17 \text{ kJ/mole}$

$\text{kcal/mole: } (+91 + +103) + (-79 + -119) = -4 \text{ kcal/mole}$

(d) break $\text{CH}_3\text{CH}_2-\text{CH}_3$ and $\text{H}-\text{H}$, make $\text{CH}_3\text{CH}_2-\text{H}$ and $\text{H}-\text{CH}_3$

$\text{kJ/mole: } (+356 + +435) + (-410 + -435) = -54 \text{ kJ/mole}$

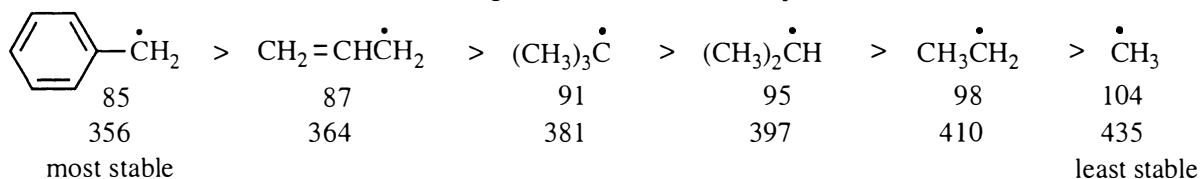
$\text{kcal/mole: } (+85 + +104) + (-98 + -104) = -13 \text{ kcal/mole}$

(e) break $\text{CH}_3\text{CH}_2-\text{OH}$ and $\text{H}-\text{Br}$, make $\text{CH}_3\text{CH}_2-\text{Br}$ and $\text{H}-\text{OH}$

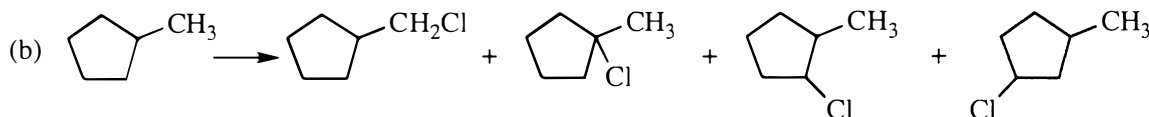
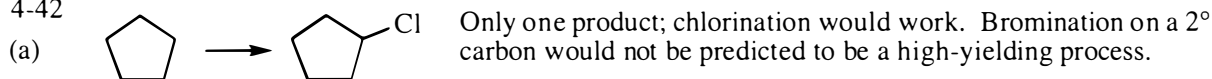
$\text{kJ/mole: } (+381 + +368) + (-285 + -498) = -34 \text{ kJ/mole}$

$\text{kcal/mole: } (+91 + +88) + (-68 + -119) = -8 \text{ kcal/mole}$

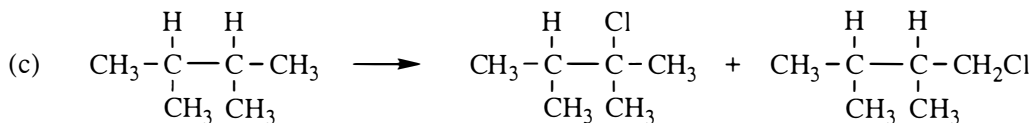
4-41 Numbers are bond dissociation energies in kcal/mole in the top line and kJ/mole in the bottom line.



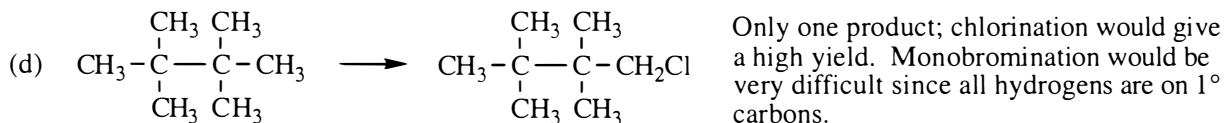
4-42



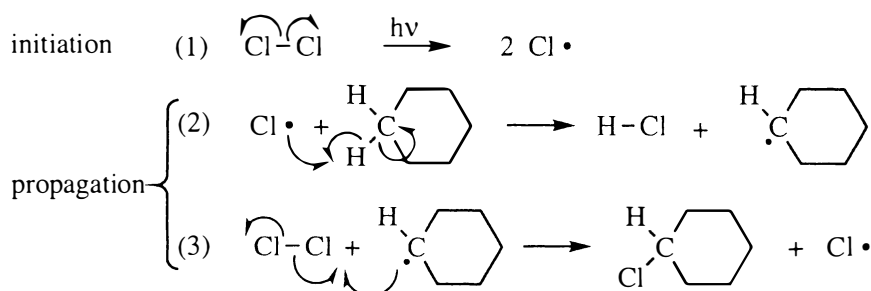
Chlorination would produce four constitutional isomers and would not be a good method to make only one of these. Monobromination at the 3° carbon would give a reasonable yield.



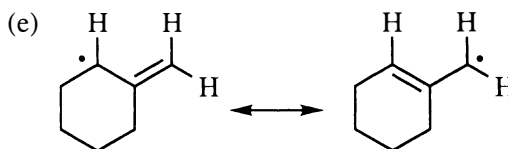
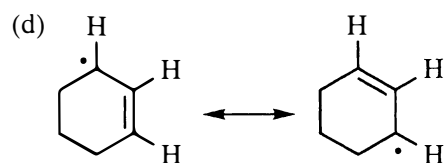
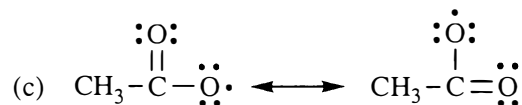
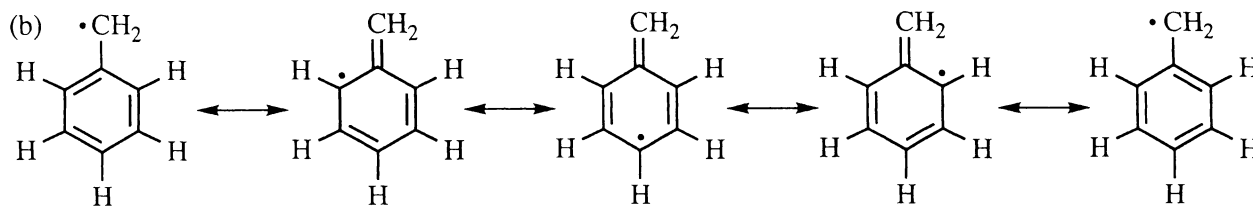
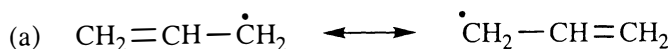
Chlorination would produce two constitutional isomers and would not be a good method to make only one of these. Monobromination would be selective for the 3° carbon and would give an excellent yield.



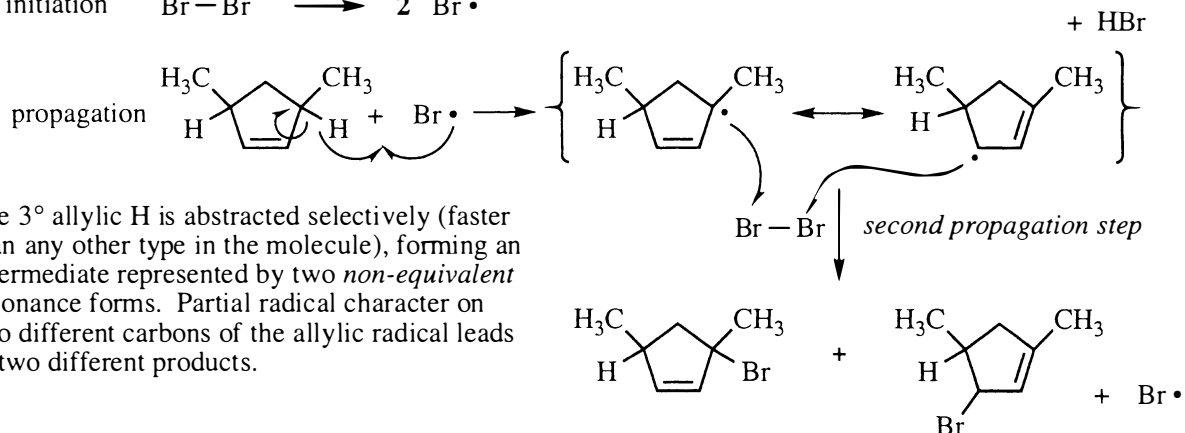
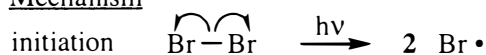
4-43



4-44

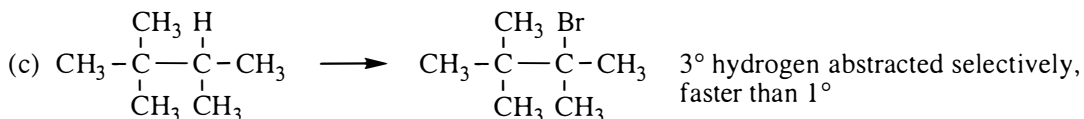
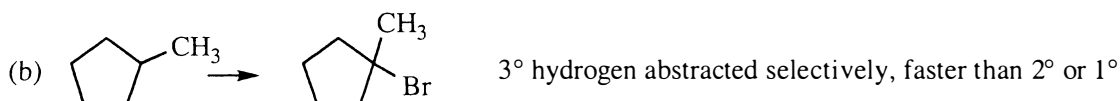
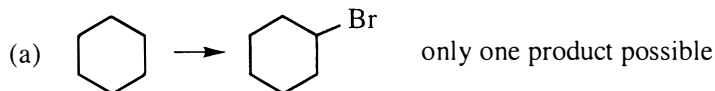


4-45

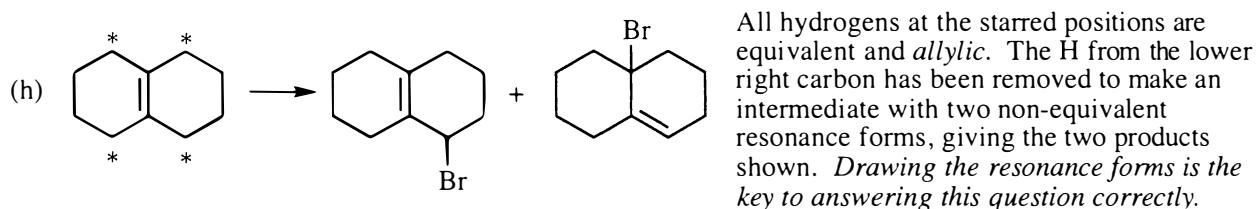
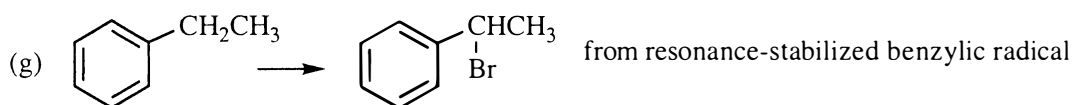
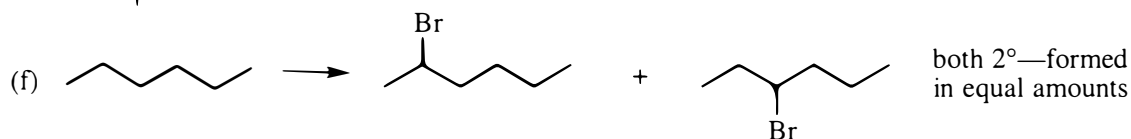
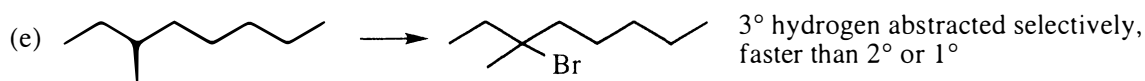
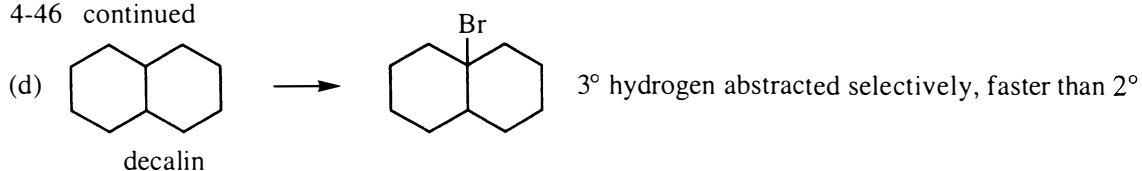
(a) Mechanism

(b) There are two reasons why the H shown is the one that is abstracted by bromine radical: the H is 3° and it is allylic, that is, neighboring a double bond. Both of these factors stabilize the radical that is created by removing the H atom.

4-46 Where mixtures are possible, only the major product is shown.



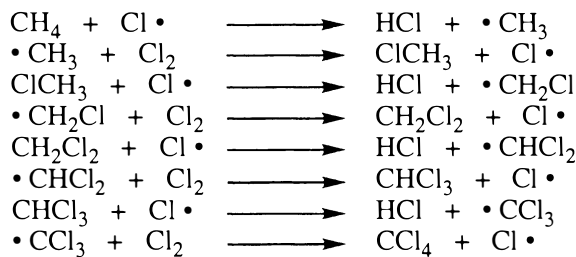
4-46 continued



4-47

(a) As CH_3Cl is produced, it can compete with CH_4 for available $\text{Cl}^\bullet$, generating CH_2Cl_2 . This can generate CHCl_3 , *etc.*

propagation steps

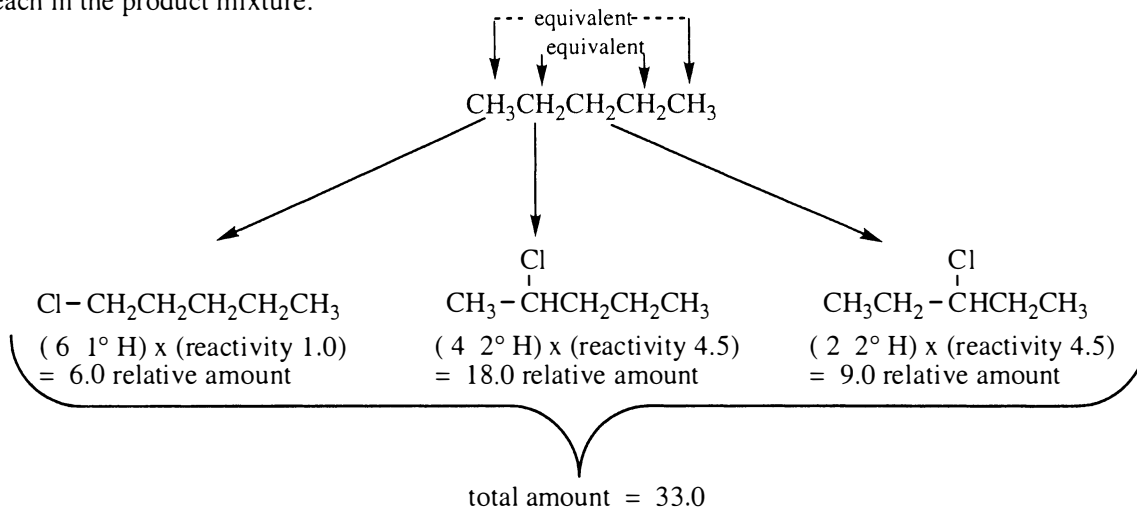


(b) To maximize CH_3Cl and minimize formation of polychloromethanes, the ratio of methane to chlorine must be kept high (see problem 4-2).

To guarantee that all hydrogens are replaced with chlorine to produce CCl_4 , the ratio of chlorine to methane must be kept high.

4-48

(a) *n*-Pentane can produce three monochloro isomers. To calculate the relative amount of each in the product mixture, multiply the numbers of hydrogens which could lead to that product times the reactivity for that type of hydrogen. Each relative amount divided by the sum of all the amounts will provide the percent of each in the product mixture.



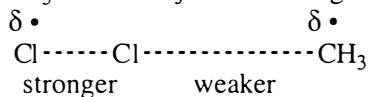
(b) $\frac{6.0}{33.0} \times 100 = 18\%$

$\frac{18.0}{33.0} \times 100 = 55\%$

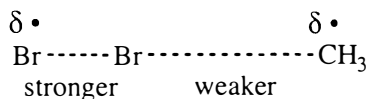
$\frac{9.0}{33.0} \times 100 = 27\%$

4-49

(a) The second propagation step in the chlorination of methane is highly exothermic ($\Delta H^\circ = -109 \text{ kJ/mole}$ (-26 kcal/mole)). The transition state resembles the reactants, that is, the Cl-Cl bond will be slightly stretched and the Cl-CH₃ bond will just be starting to form.

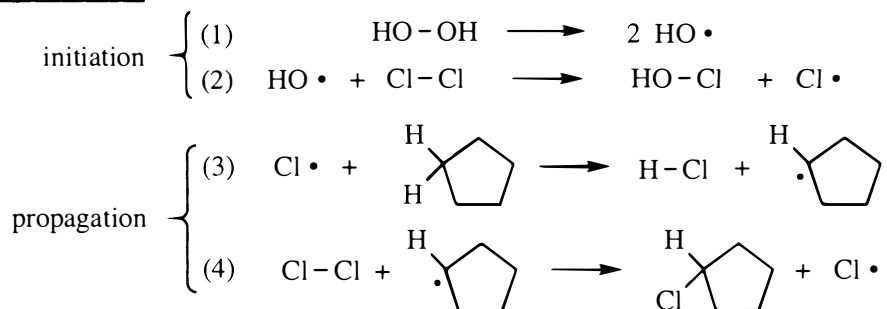


(b) The second propagation step in the bromination of methane is highly exothermic ($\Delta H^\circ = -101 \text{ kJ/mole}$ (-24 kcal/mole)). The transition state resembles the reactants, that is, the Br-Br bond will be slightly stretched and the Br-CH₃ bond will just be starting to form.

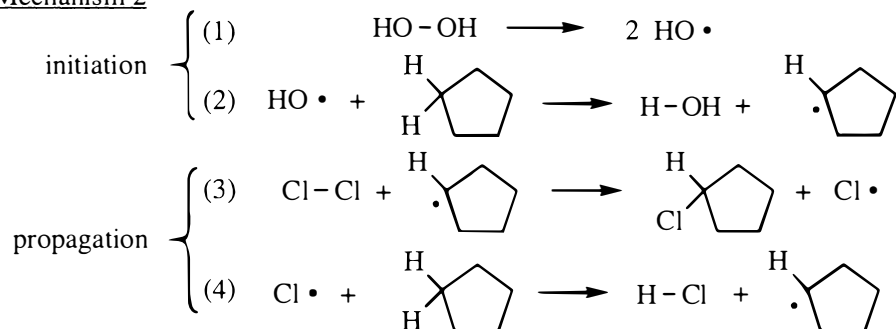


4-50 Two mechanisms are possible depending on whether $\text{HO} \cdot$ reacts with chlorine or with cyclopentane.

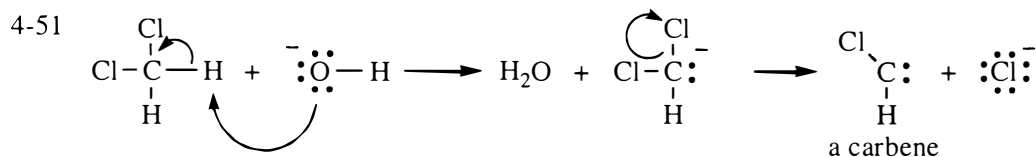
Mechanism 1



Mechanism 2



The energies of the propagation steps determine which mechanism is followed. The bond dissociation energy of $\text{HO}-\text{Cl}$ is about 210 kJ/mole (about 50 kcal/mole), making initiation step (2) in mechanism 1 *endothermic* by about 30 kJ/mole (about 8 kcal/mole). In mechanism 2, initiation step (2) is *exothermic* by about 101 kJ/mole (24 kcal/mole); mechanism 2 is preferred.



4-52 This critical equation is the key to this problem: $\Delta G = \Delta H - T \Delta S$

At 1400 K, the equilibrium constant is 1; therefore:

$$K_{\text{eq}} = 1 \quad \Longrightarrow \quad \Delta G = 0 \quad \Longrightarrow \quad \Delta H = T \Delta S$$

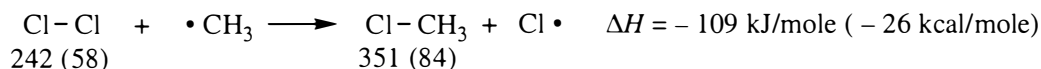
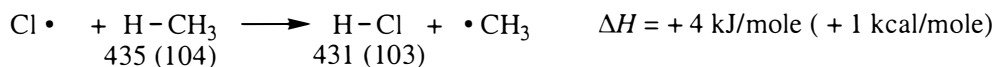
Assuming ΔH is about the same at 1400 K as it is at calorimeter temperature:

$$\begin{aligned} \Delta S &= \frac{\Delta H}{T} = \frac{-137 \text{ kJ/mole}}{1400 \text{ K}} = \frac{-137,000}{1400} \text{ J/K-mole} \\ &= -98 \text{ J/K-mole} \quad (-23 \text{ cal/K-mole}) \end{aligned}$$

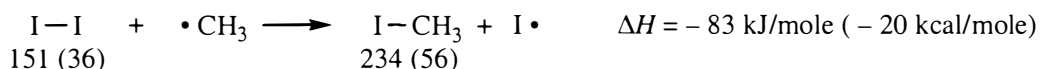
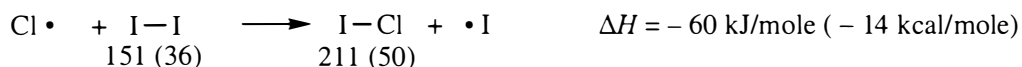
This is a large *decrease* in entropy, consistent with two molecules combining into one.

4-53

Assume that chlorine atoms (radicals) are still generated in the initiation reaction. Focus on the propagation steps. Bond dissociation energies are given below the bonds, in kJ/mole (kcal/mole).

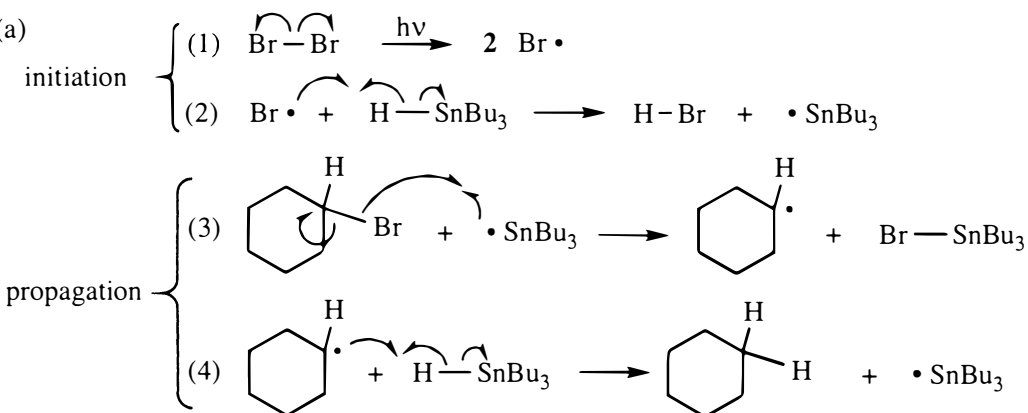


What happens when the different radical species react with iodine?



Compare the second reaction in each pair: methyl radical reacting with chlorine is more exothermic than methyl radical reacting with iodine; this does not explain how iodine prevents the chlorination reaction. Compare the first reaction in each pair: chlorine atom reacting with iodine is very exothermic whereas chlorine atom reacting with methane is slightly endothermic. Here is the key: chlorine atoms will be scavenged by iodine before they have a chance to react with methane. Without chlorine atoms, the reaction comes to a dead stop.

4-54 (a)



(b) All energies are in kJ/mole. The abbreviation "cy" stands for the cyclohexane ring.

Step 2: break H—Sn, make H—Br: $+310 + -368 = -58 \text{ kJ/mole}$

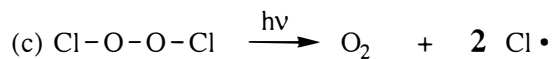
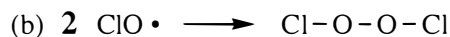
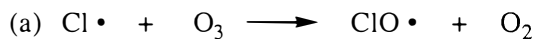
Step 3: break cy—Br, make Br—Sn: $+285 + -552 = -267 \text{ kJ/mole}$ WOW!

Step 4: break H—Sn, make cy—H: $+310 + -397 = -87 \text{ kJ/mole}$

The sum of the two propagation steps are: $-267 + -87 = -354 \text{ kJ/mole}$ —a hugely exothermic reaction.

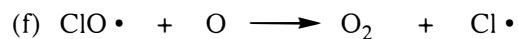
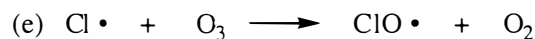
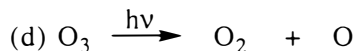
4-55

Mechanism 1:



The biggest problem in Mechanism 1 lies in step (b). The concentration of Cl atoms is very small, so at any given time, the concentration of ClO will be very small. The probability of two ClO radicals finding each other to form ClOOC1 is virtually zero. Even though this mechanism shows a catalytic cycle with Cl• (starting the mechanism and being regenerated at the end), the middle step makes it highly unlikely.

Mechanism 2:

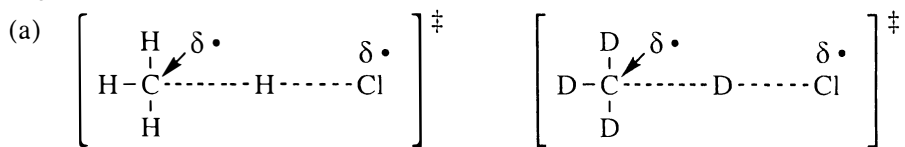


Step (d) is the "light" reaction that occurs naturally in daylight. At night, the reaction reverses and regenerates ozone.

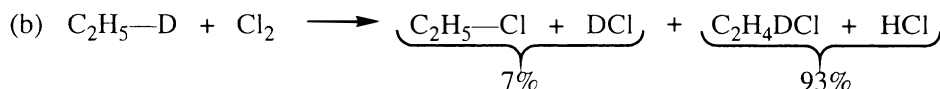
Step (f) is the crucial step. A low concentration of ClO *will* find a relatively high concentration of O atoms because the "light" reaction is producing O atoms in relative abundance. Cl• is regenerated and begins propagation step (e), continuing the catalytic cycle.

Mechanism 2 is believed to be the dominant mechanism in ozone depletion. Mechanism 1 can be discounted because of the low probability of step (b) occurring, because two species in very low, catalytic concentration are required to find each other in order for the step to occur.

4-56



In each case, the bond from carbon to H (D) is breaking and the bond from H (D) to Cl is forming.



D replacement: $7\% \div 1 \text{ D} = 7$ (reactivity factor)

H replacement: $93\% \div 5 \text{ H} = 18.6$ (reactivity factor)

relative reactivity of H : D abstraction = $18.6 \div 7 = 2.7$

Each hydrogen is abstracted 2.7 times faster than deuterium.

(c) In both reactions of chlorine with either methane or ethane, the first propagation step is rate-limiting. The reaction of chlorine atom with methane is *endothermic* by 4 kJ/mole (1 kcal/mole), while for ethane this step is *exothermic* by 21 kJ/mole (5 kcal/mole). By the Hammond Postulate, differences in activation energy are most pronounced in *endothermic* reactions where the transition states most resemble the products. Therefore, a change in the methane molecule causes a greater change in its transition state energy than the same change in the ethane molecule causes in its transition state energy. Deuterium will be abstracted more slowly in both methane and ethane, but the rate effect will be more pronounced in methane than in ethane.

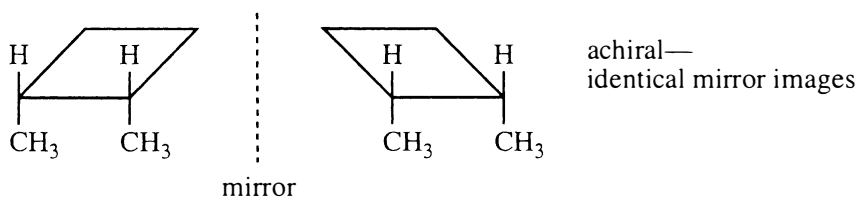
CHAPTER 5—STEREOCHEMISTRY

Note to the student: Stereochemistry is the study of molecular structure and reactions in three dimensions. Molecular models will be especially helpful in this chapter.

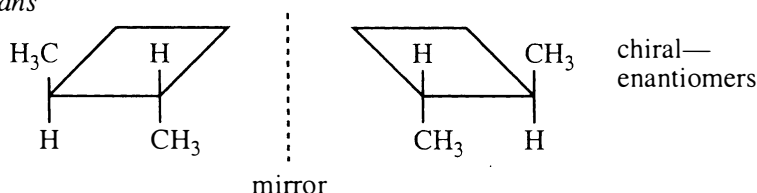
5-1 The best test of whether a household object is chiral is whether it would be used equally well by a left- or right-handed person. The chiral objects are the corkscrew, the writing desk, the screw-cap bottle (only for refilling, however; in use, it would not be chiral), the rifle and the knotted rope; the corkscrew, the bottle top, and the rope each have a twist in one direction, and the rifle and desk are clearly made for right-handed users. All the other objects are achiral and would feel equivalent to right- or left-handed users.

5-2

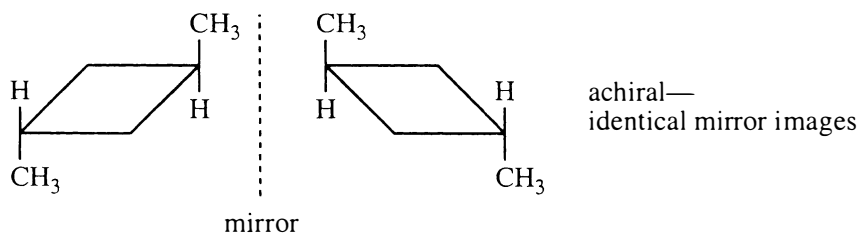
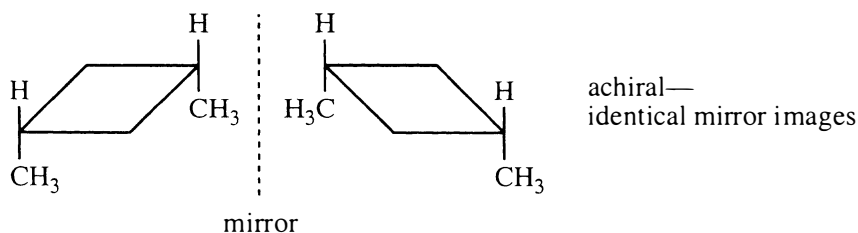
(a) *cis*



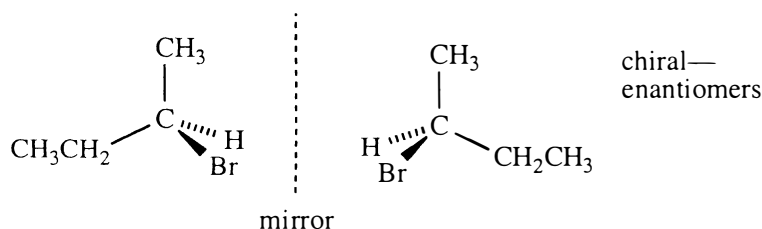
(b) *trans*



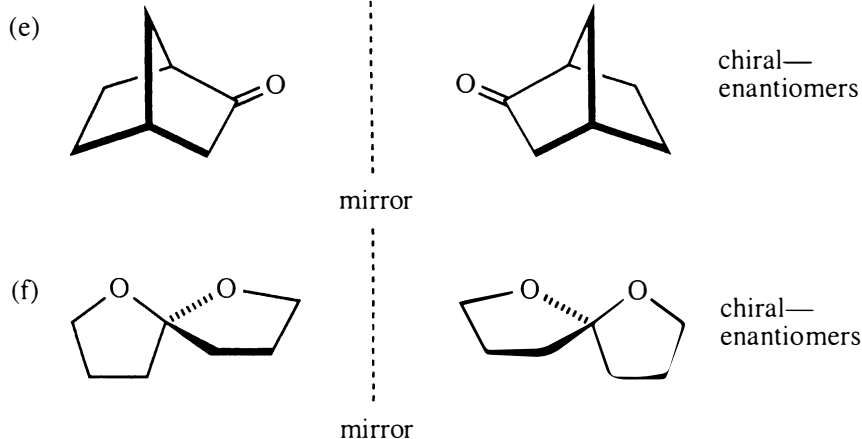
(c) *cis* first, then *trans*



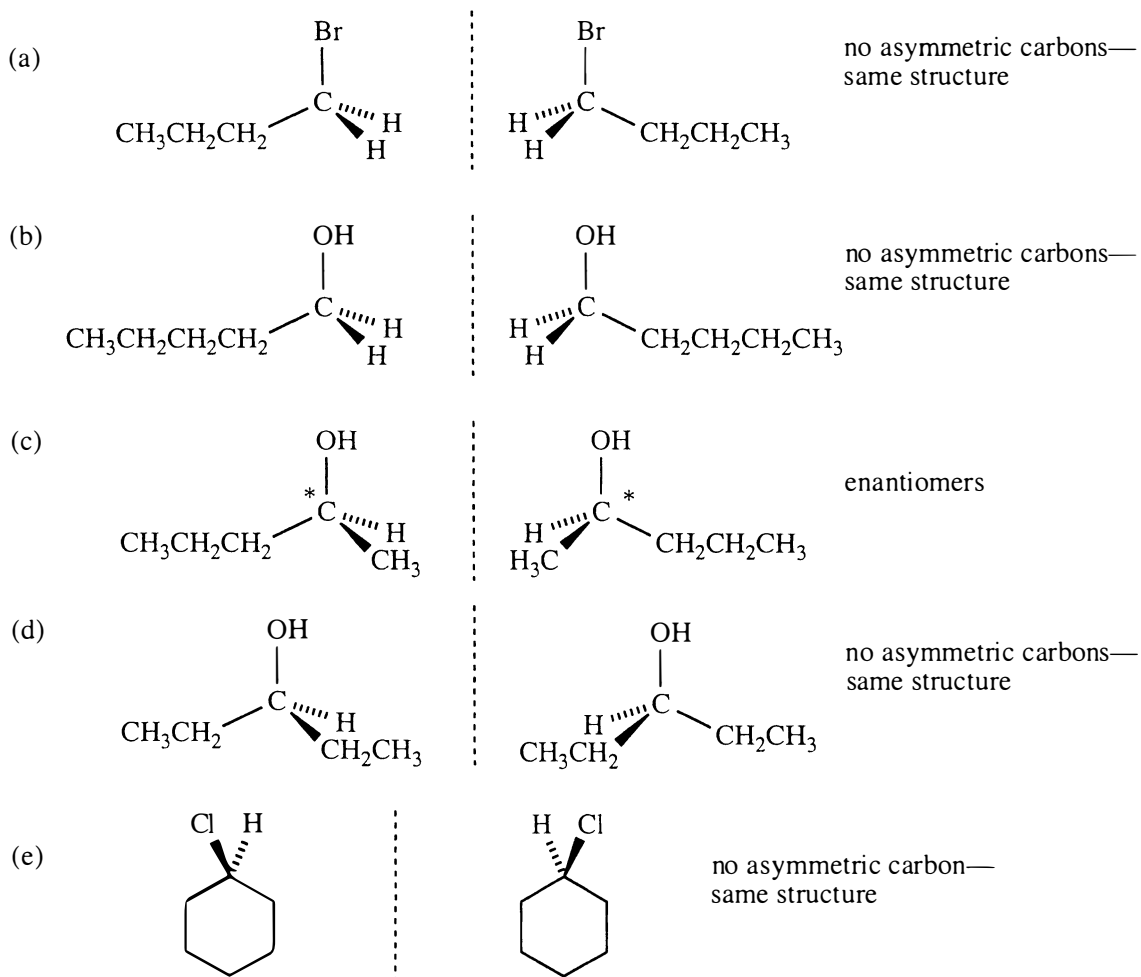
(d)



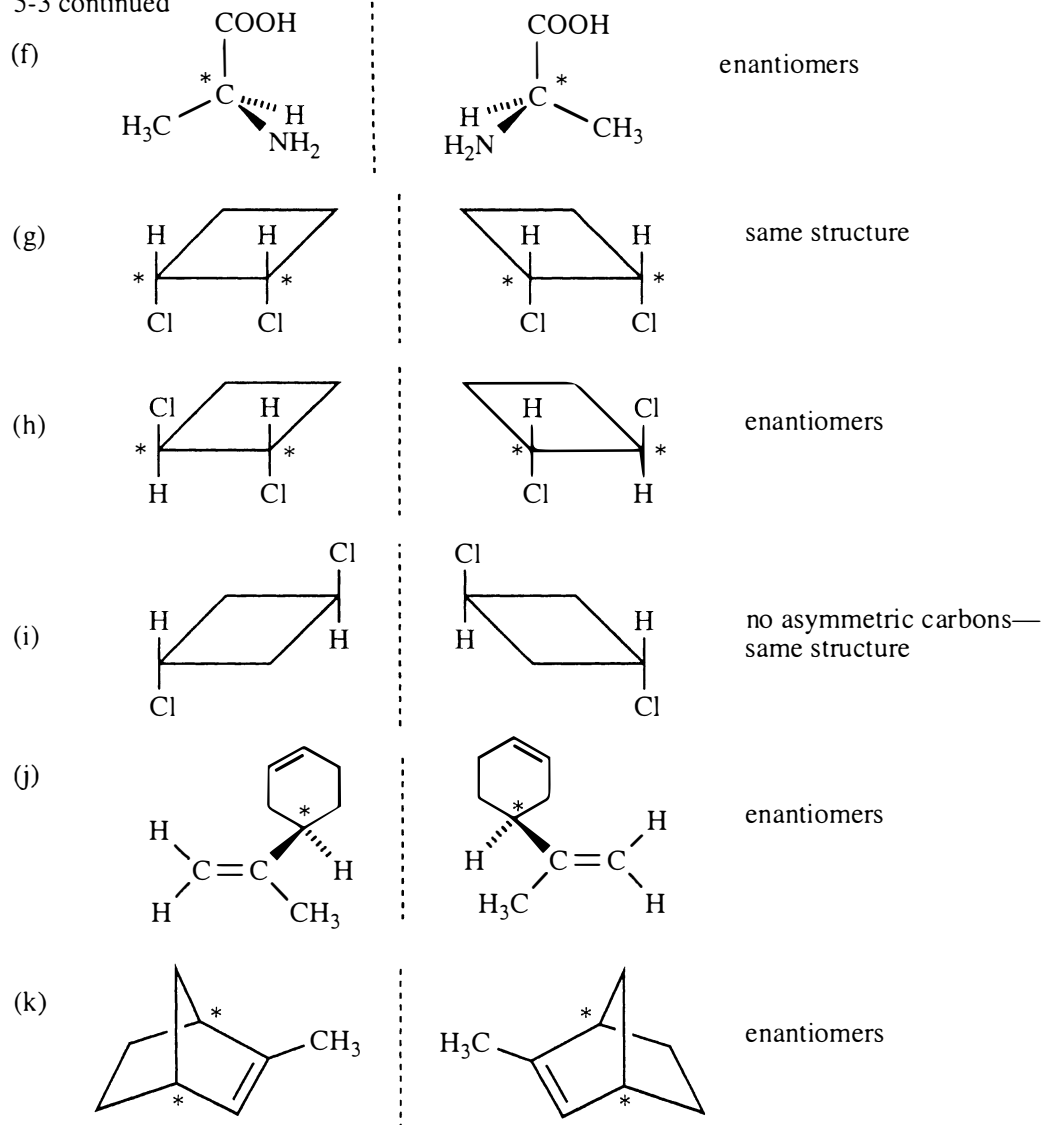
5-2 continued



5-3 Asymmetric carbon atoms are starred.

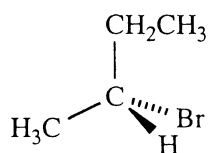


5-3 continued

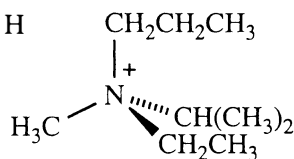


5-4 You may have chosen to interchange two groups different from the ones shown here. The type of isomer produced will still be the same as listed here.

Interchanging any two groups around a chirality center will create an enantiomer of the first structure.

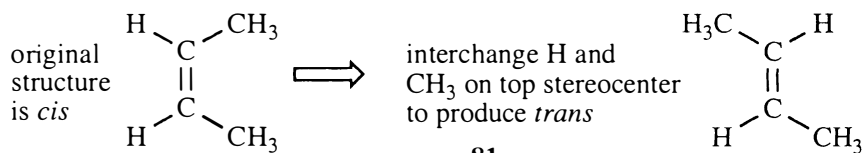


Interchanging the Br and the H creates an enantiomer of the structure in Figure 5-5.



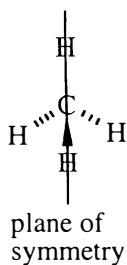
Interchanging the ethyl and the isopropyl creates an enantiomer of the structure in Figure 5-5.

On a double bond, interchanging the two groups on ONE of the stereocenters will create the other geometric (*cis-trans*) isomer. However, interchanging the two groups on BOTH of the stereocenters will give the original structure.

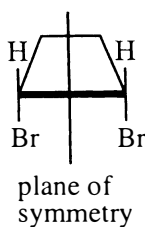


5-5

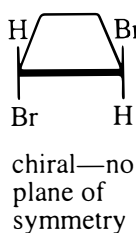
(a)



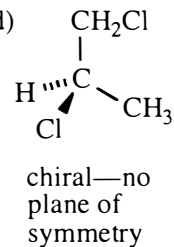
(b)



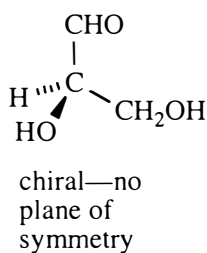
(c)



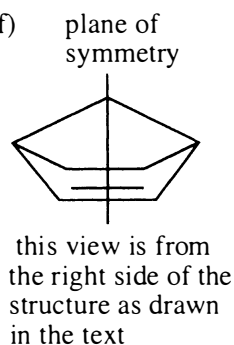
(d)



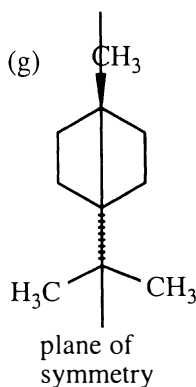
(e)



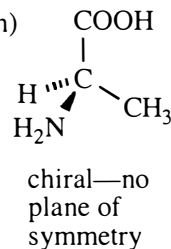
(f)



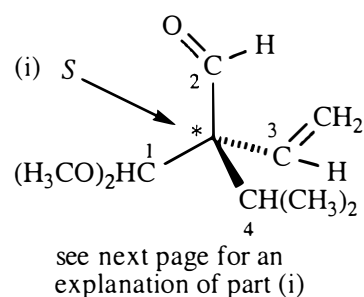
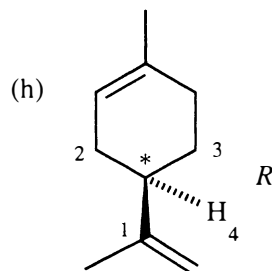
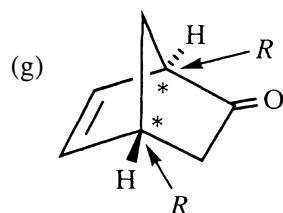
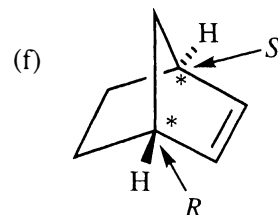
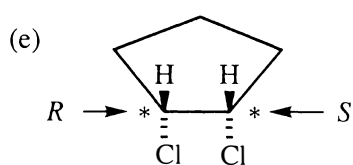
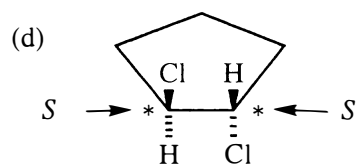
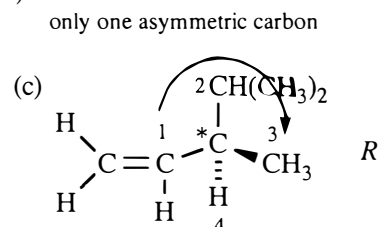
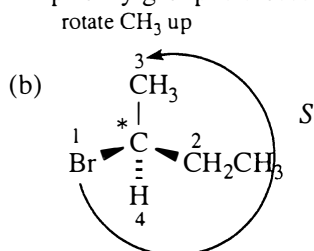
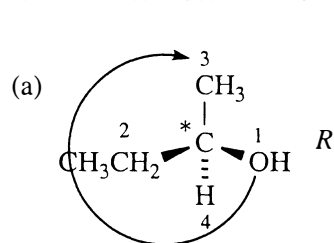
(g)



(h)

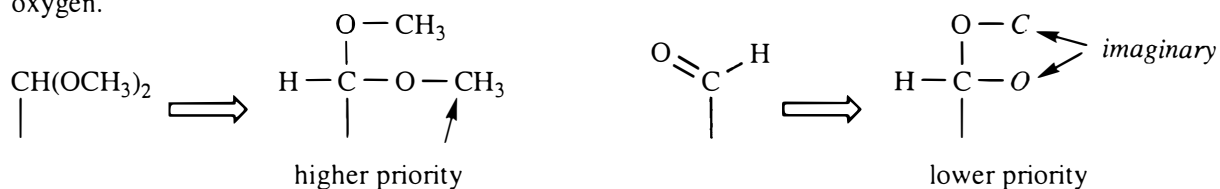


5-6 ALWAYS place the 4th priority group away from you. Then determine if the sequence 1→2→3 is clockwise (*R*) or counter-clockwise (*S*). (There is a Problem-Solving Hint near the end of section 5-3 in the text that describes what to do when the 4th priority group is closest to you.)

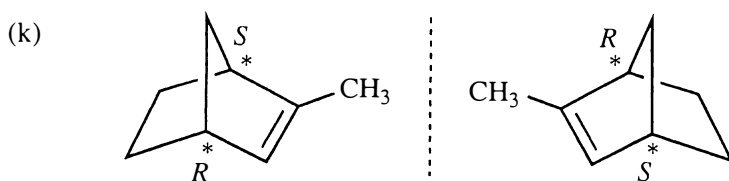
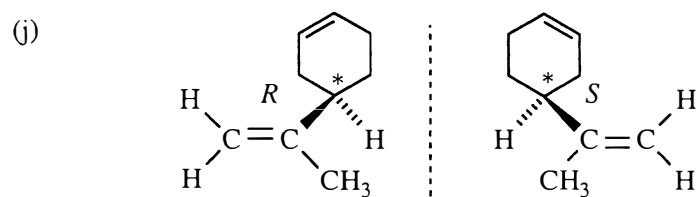
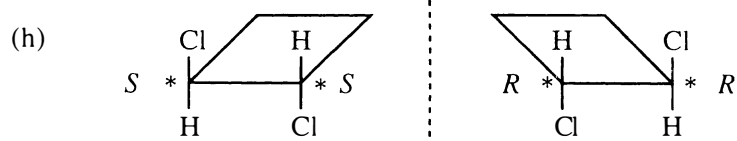
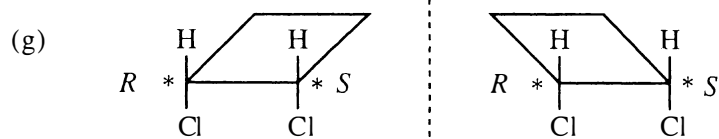
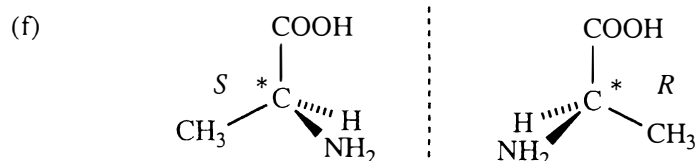
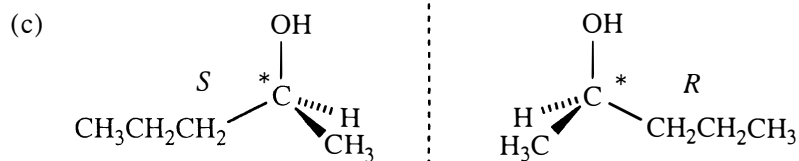


5-6 continued

Part (i) deserves some explanation. The difference between groups 1 and 2 hinge on what is on the "extra" oxygen.



5-7 There are no asymmetric carbons in 5-3 (a), (b), (d), (e), or (i).



5-8

2.0 g / 10 mL = 0.20 g/mL ; 100 mm = 1 dm

$$[\alpha]_D^{25} = \frac{+1.74^\circ}{(0.20)(1)} = +8.7^\circ \text{ for (+)-glyceraldehyde}$$

5-9

0.5 g / 10 mL = 0.05 g/mL ; 20 cm = 2 dm

$$[\alpha]_D^{25} = \frac{-5.0^\circ}{(0.05)(2)} = -50^\circ \text{ for (-)-epinephrine}$$

5-10

Measure using a solution of about one-fourth the concentration of the first. The value will be either + 45° or - 45°, which gives the sign of the rotation.

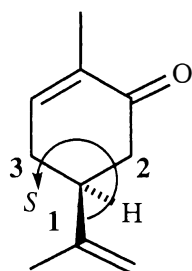
5-11

Whether a sample is dextrorotatory (abbreviated "(+)") or levorotatory (abbreviated "(-)") is determined experimentally by a polarimeter. Except for the molecule glyceraldehyde, there is no direct, universal correlation between direction of optical rotation ((+) and (-)) and designation of configuration (*R* and *S*). In other words, one dextrorotatory compound might have *R* configuration while a different dextrorotatory compound might have *S* configuration.

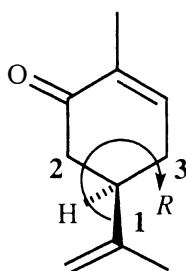
(a) Yes, both of these are determined experimentally: the (+) or (-) by the polarimeter and the smell by the nose.

(b) No, *R* or *S* cannot be determined by either the polarimeter or the nose.

(c) The drawings show that (+)-carvone from caraway has the *S* configuration and (-)-carvone from spearmint has the *R* configuration.



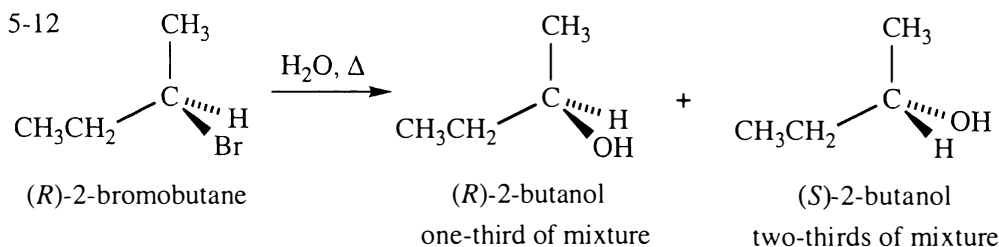
(+)-carvone (caraway seed)



(-)-carvone (spearmint)

(For fun, ask your instructor if you can smell the two enantiomers of carvone. Some people are unable, presumably for genetic reasons, to distinguish the fragrance of the two enantiomers.)

5-12



Chapter 6 will explain how these mixtures come about. For this problem, the *S* enantiomer accounts for 66.7% of the 2-butanol in the mixture and the rest, 33.3%, is the *R* enantiomer. Therefore, the excess of one enantiomer over the racemic mixture must be 33.3% of the *S*, the enantiomeric excess. (All of the *R* is "canceled" by an equal amount of the *S*, algebraically as well as in optical rotation.)

The optical rotation of pure (*S*)-2-butanol is + 13.5°. The optical rotation of this mixture is:
 $33.3\% \times (+13.5^\circ) = +4.5^\circ$

5-13 The rotation of pure (+)-2-butanol is $+13.5^\circ$.

$$\frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} = \frac{+0.45^\circ}{+13.5^\circ} \times 100\% = 3.3\% \text{ optical purity}$$

$$= 3.3\% \text{ e.e.} = \text{excess of (+) over (-)}$$

To calculate percentages of (+) and (-): (two equations in two unknowns)

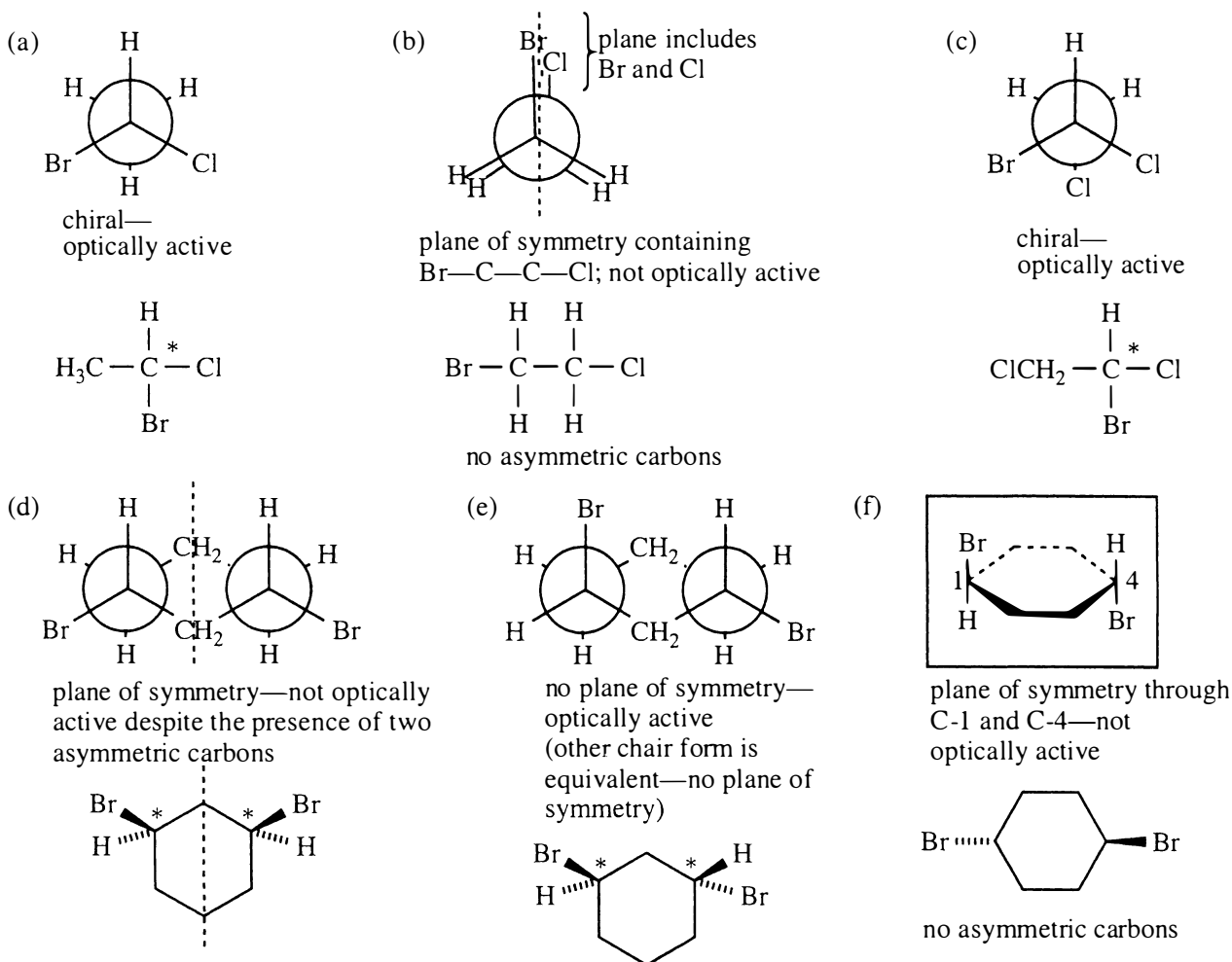
$$(+)+(-)=100\% \implies (-)=100\%-(+)$$

$$(+)-(-)=3.3\% \implies (+)-(100\%-(+))=3.3\%$$

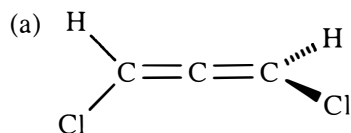
$$2(+)=103.3\%$$

$$\begin{aligned} (+) &= 51.6\% \text{ (rounded)} \\ (-) &= 48.4\% \end{aligned}$$

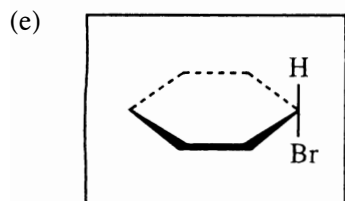
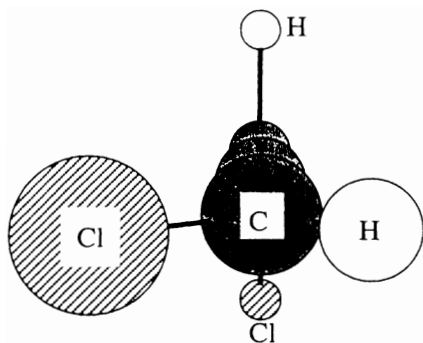
5-14 Drawing Newman projections is the clearest way to determine symmetry of conformations.



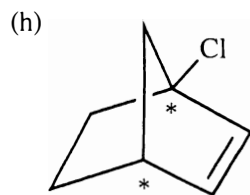
Part (2) Predictions of optical activity based on asymmetric centers give the same answers as predictions based on the most symmetric conformation.



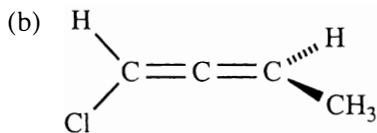
no asymmetric carbons, but the molecule is chiral (an allene); the drawing below is a three-dimensional picture of the allene in (a) showing there is no plane of symmetry because the substituents of an allene are in different planes



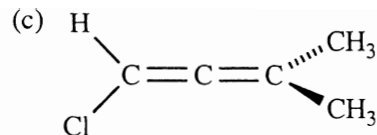
plane of symmetry bisecting the molecule; no asymmetric carbons; not a chiral molecule



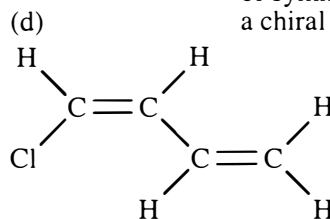
two asymmetric carbons; a chiral compound



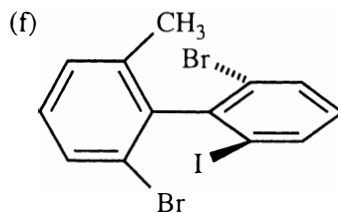
no asymmetric carbons, but the molecule is chiral (an allene)



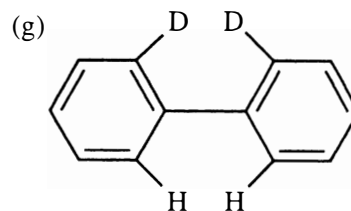
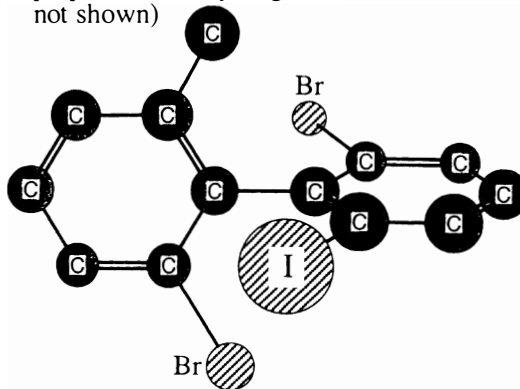
no asymmetric carbons; this allene has a plane of symmetry between the two methyls (the plane of the paper), including all the other atoms because the two pi bonds of an allene are perpendicular, the Cl is in the plane of the paper and the plane of symmetry goes through it; not a chiral molecule



planar molecule—no asymmetric carbons; not a chiral molecule

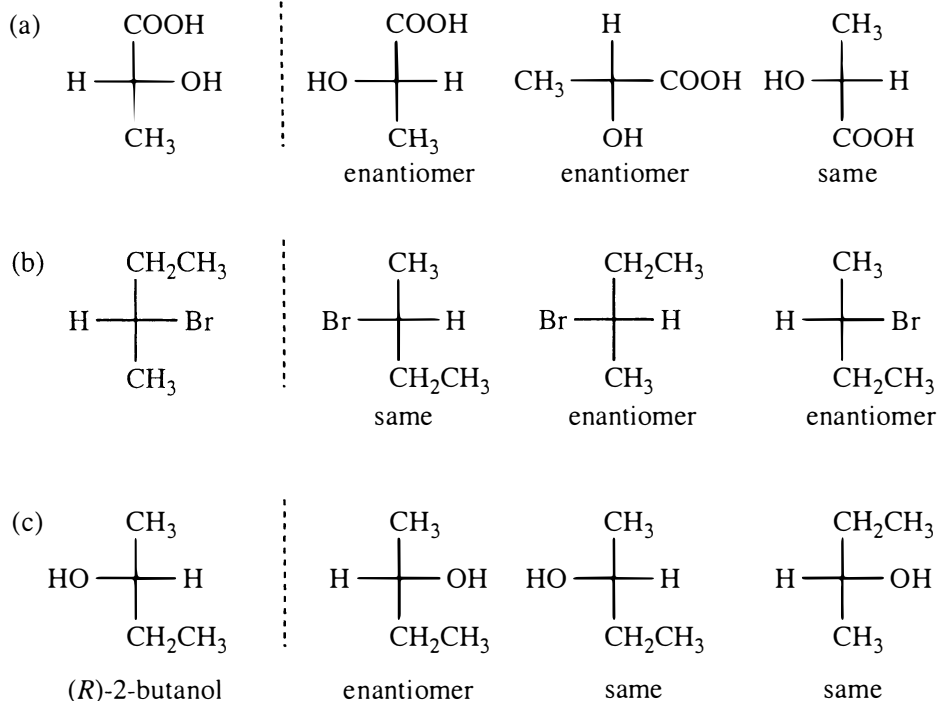


no asymmetric carbons, but the molecule is chiral due to restricted rotation; the drawing below is a three-dimensional picture showing that the rings are perpendicular (hydrogens are not shown)



no asymmetric carbons, and the groups are not large enough to restrict rotation; not a chiral compound

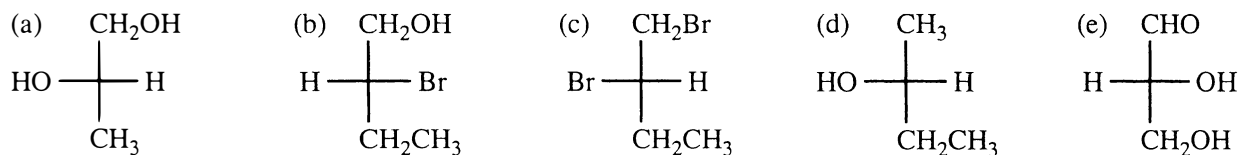
5-16

**Rules for Fischer projections:**

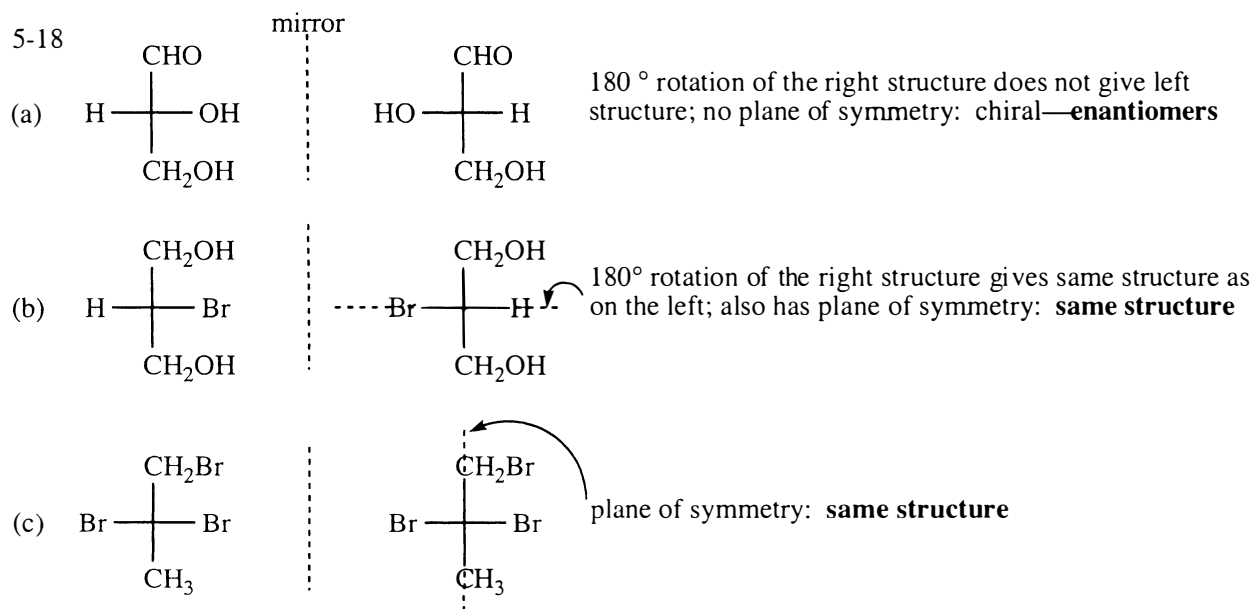
1. Interchanging any two groups an odd number of times (once, three times, etc.) makes an enantiomer. Interchanging any two groups an even number of times (e.g. twice) returns to the original stereoisomer.

2. Rotating the structure by 90° makes the enantiomer. Rotating by 180° returns to the original stereoisomer. (The second rule is an application of the first. Prove this to yourself.)

5-17

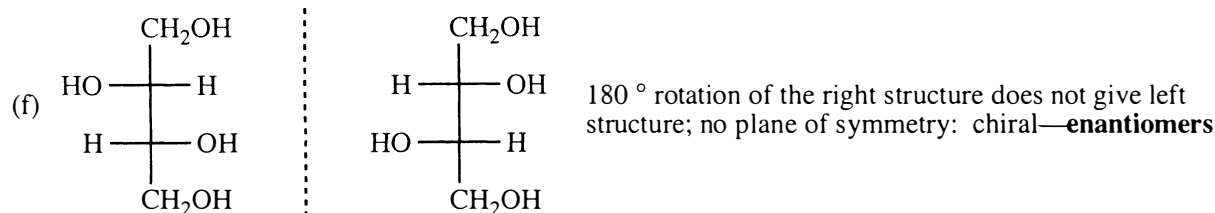
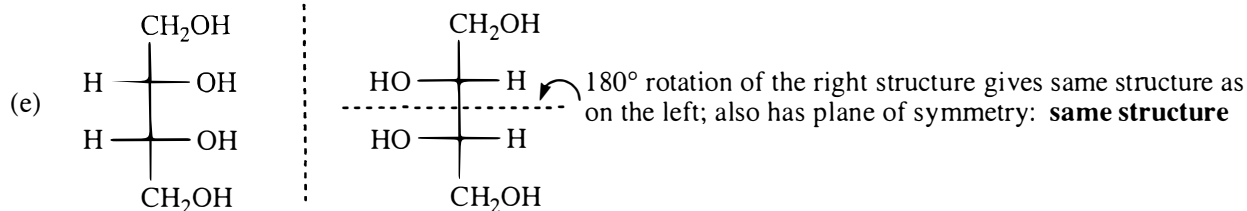
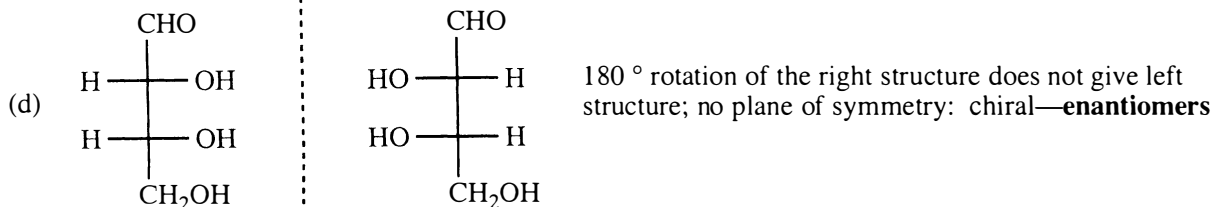


5-18



5-18 continued

mirror



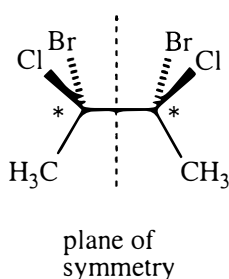
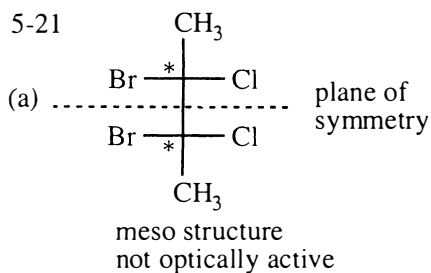
5-19 If the Fischer projection is drawn correctly, the most oxidized carbon will be at the top; this is the carbon with the greatest number of bonds to oxygen. Then the numbering goes from the top down.

- | | | |
|----------------------|---|--------------|
| (a) <i>R</i> | (d) 2 <i>R</i> ,3 <i>R</i> | (g) <i>R</i> |
| (b) no chiral center | (e) 2 <i>S</i> ,3 <i>R</i> (numbering down) | (h) <i>S</i> |
| (c) no chiral center | (f) 2 <i>R</i> , 3 <i>R</i> | (i) <i>S</i> |

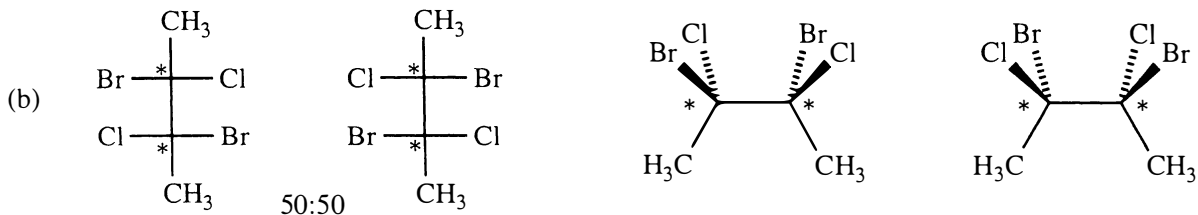
5-20

- (a) enantiomers—configurations at both asymmetric carbons inverted
- (b) diastereomers—configuration at only one asymmetric carbon inverted
- (c) diastereomers—configuration at only one asymmetric carbon inverted (the left carbon)
- (d) constitutional isomers—C=C shifted position
- (e) enantiomers—chiral, mirror images
- (f) diastereomers—configuration at only one asymmetric carbon inverted (the top one)
- (g) enantiomers—configuration at all asymmetric carbons inverted
- (h) same compound—superimposable mirror images (hard question! use a model)
- (i) diastereomers—configuration at only one chirality center (the nitrogen) inverted

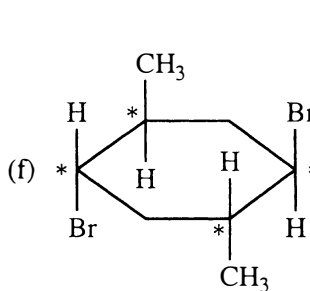
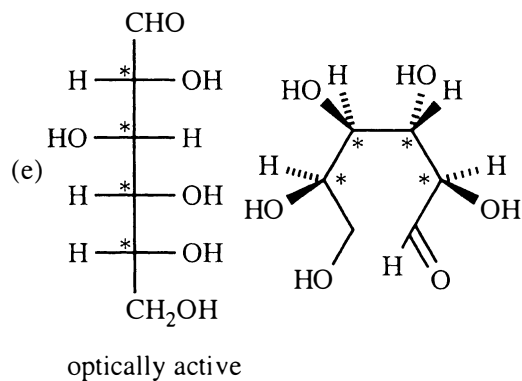
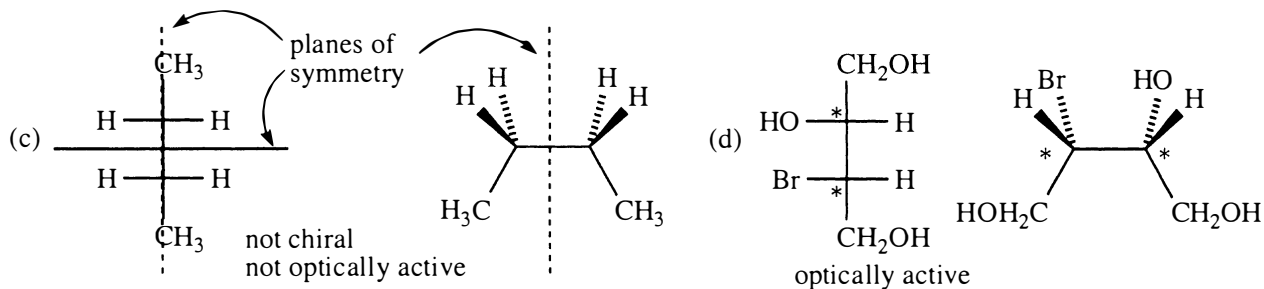
5-21



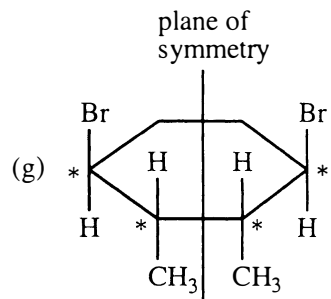
5-21 continued



racemic mixture—not optically active, although each enantiomer by itself would be optically active

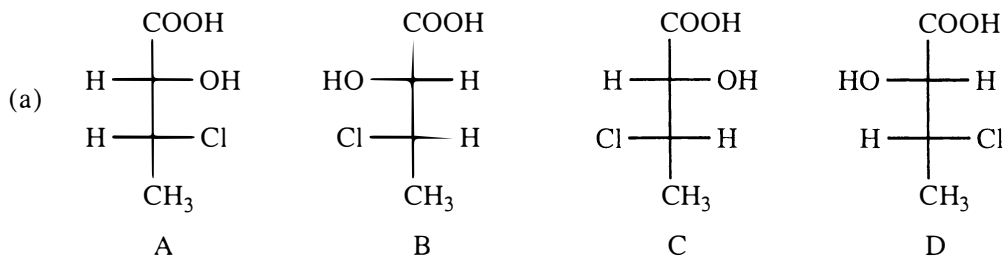


not optically active—
superimposable on its
mirror image—
technically, this is
a meso structure
(may require models!)



meso—
not optically active

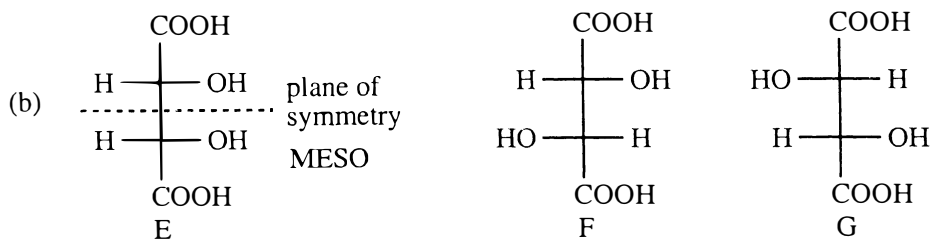
5-22



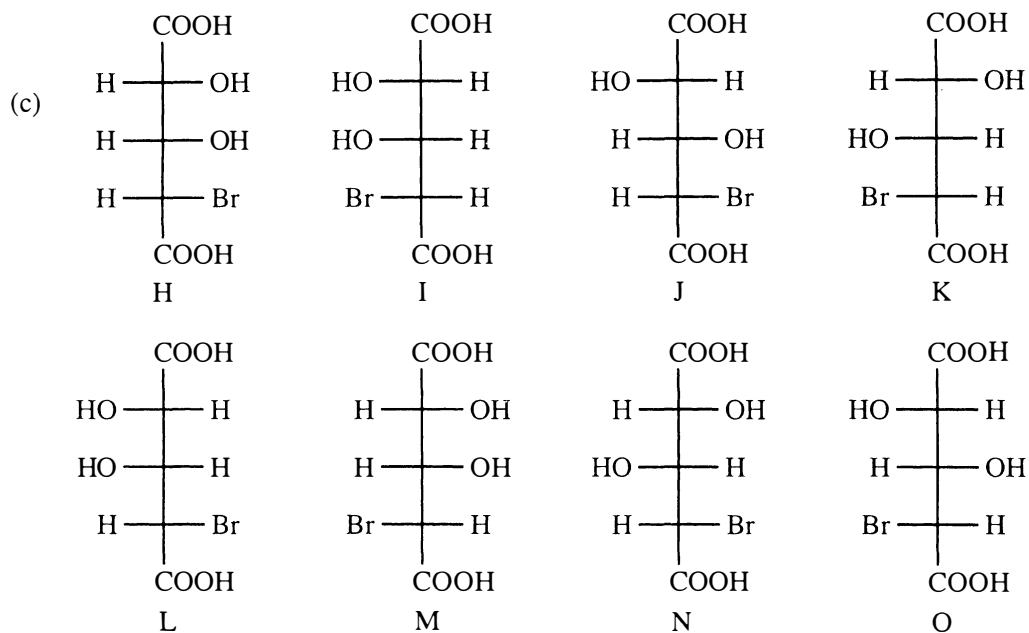
enantiomers: A and B; C and D

diastereomers: A and C; A and D; B and C; B and D

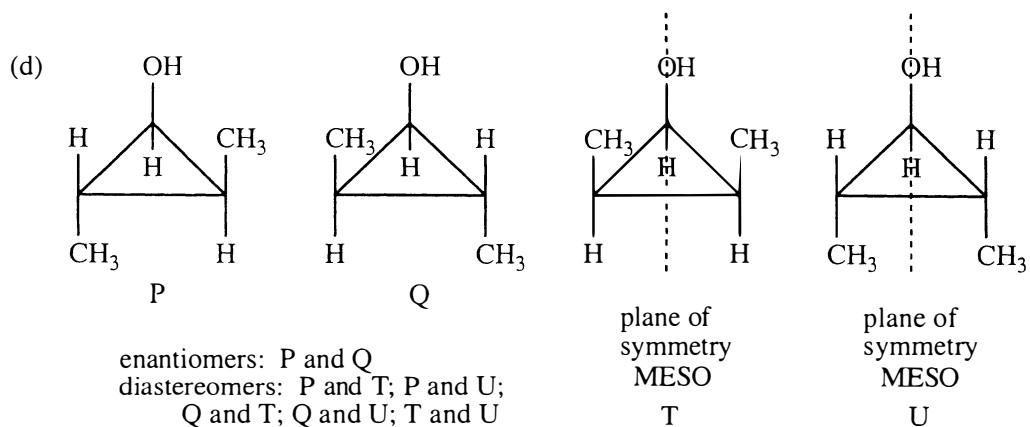
5-22 continued



enantiomers: F and G
diastereomers: E and F; E and G

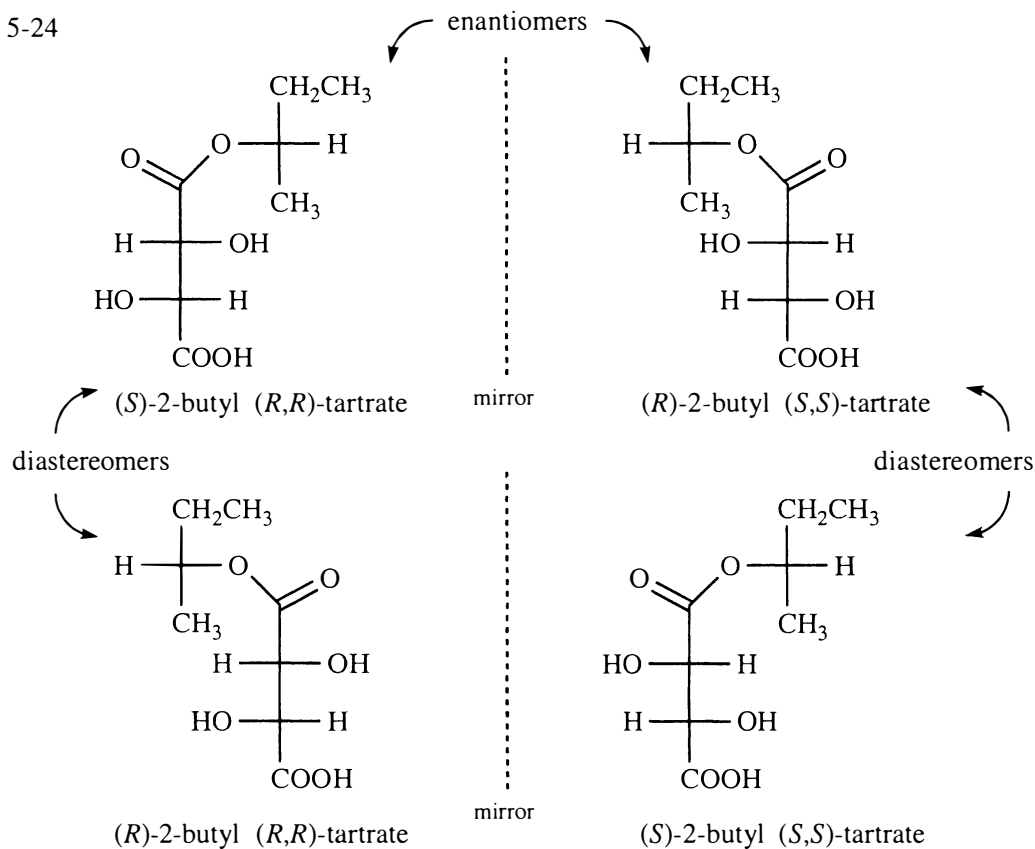


enantiomers: H and I; J and K; L and M; N and O
diastereomers: any pair which is not enantiomeric



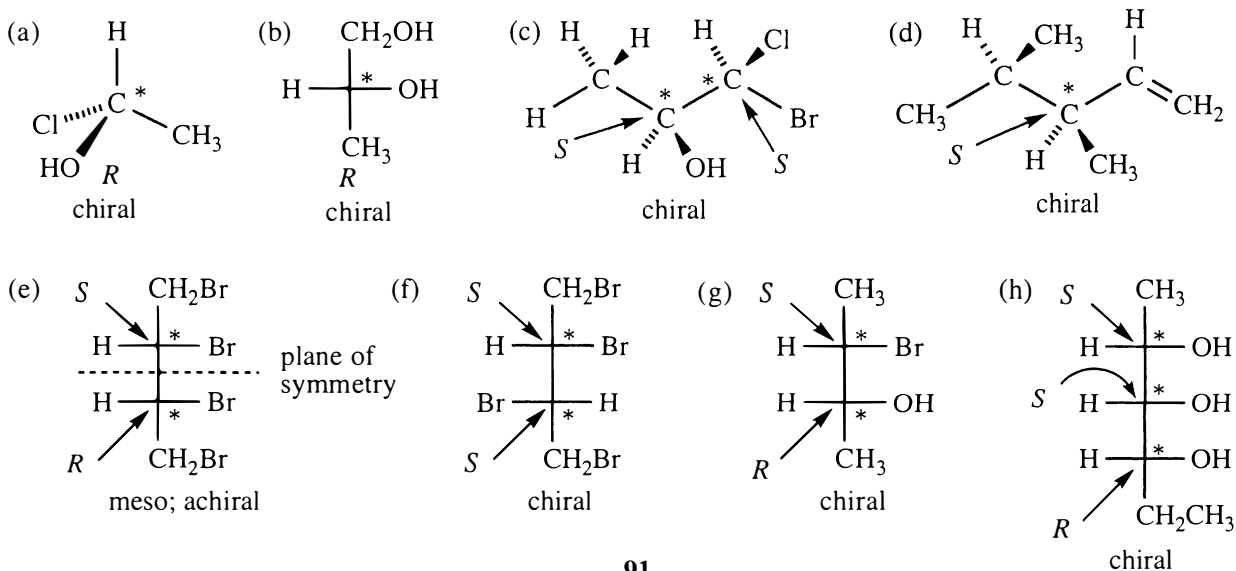
5-23 Any diastereomeric pair could be separated by a physical process like distillation or crystallization. Diastereomers are found in parts (a), (b), and (d). The structures in (c) are enantiomers; they could not be separated by normal physical means.

5-24

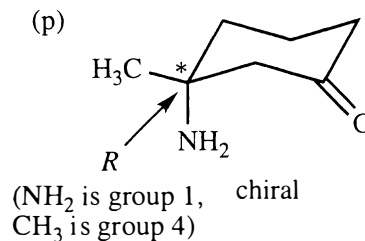
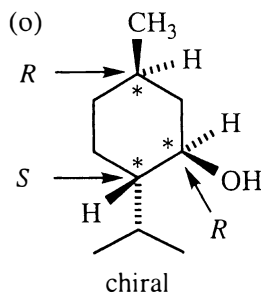
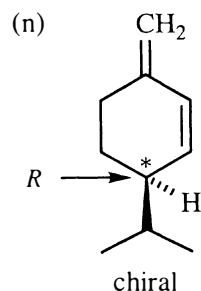
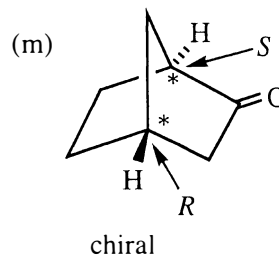
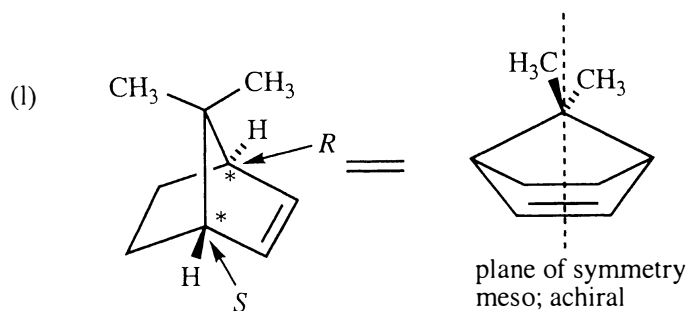
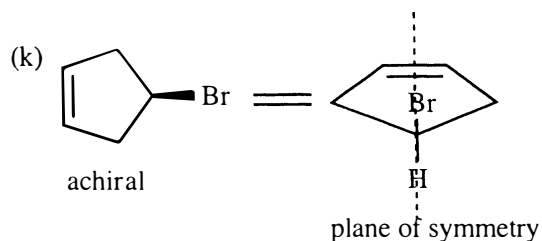
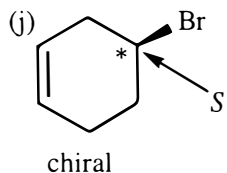
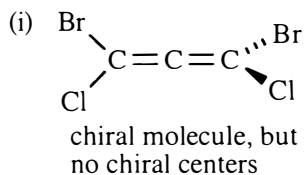


5-25 Please refer to solution 1-20, page 12 of this Solutions Manual.

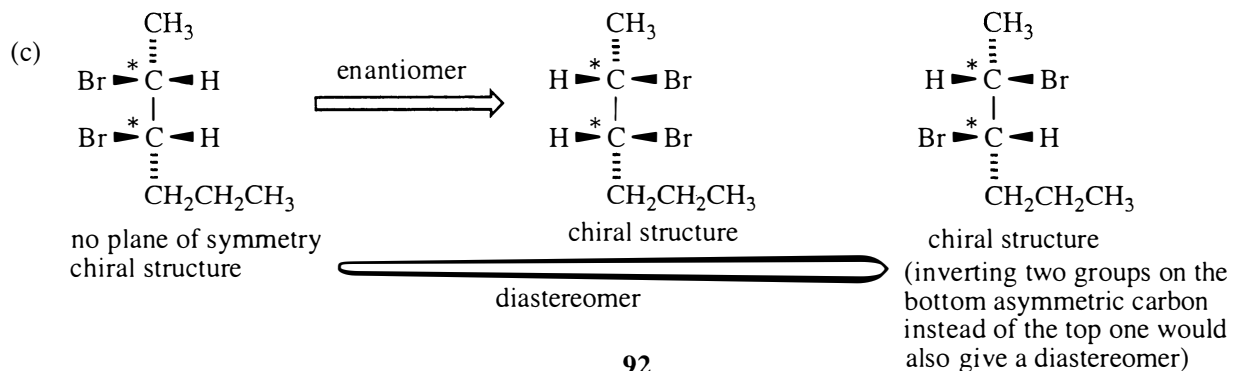
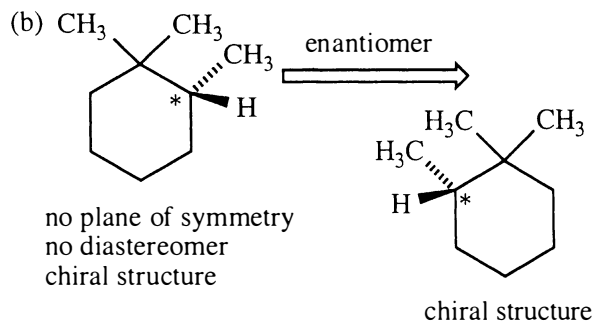
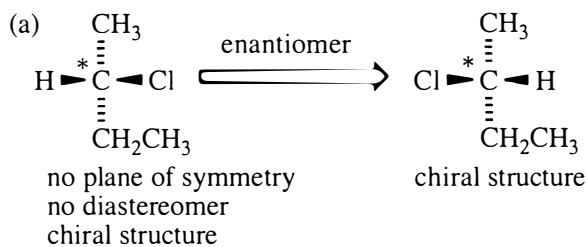
5-26



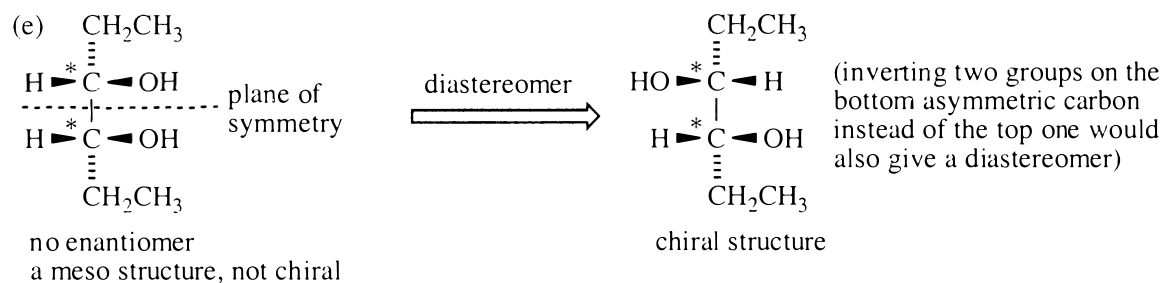
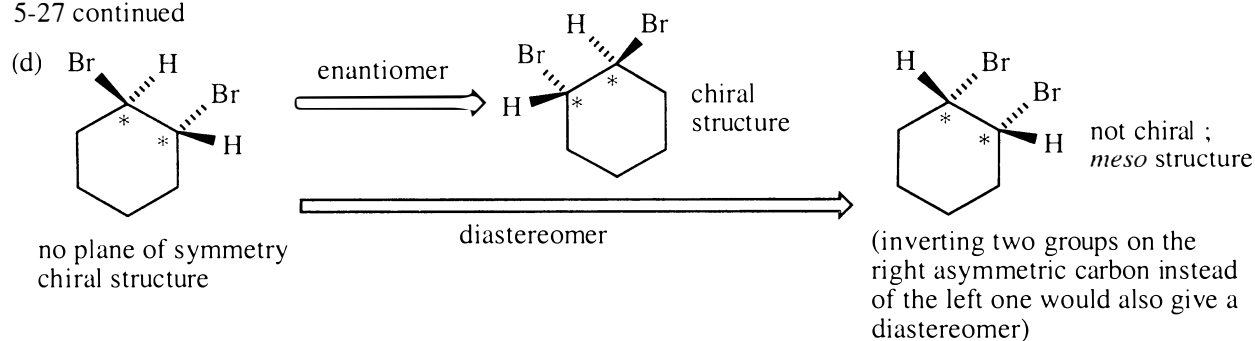
5-26 continued



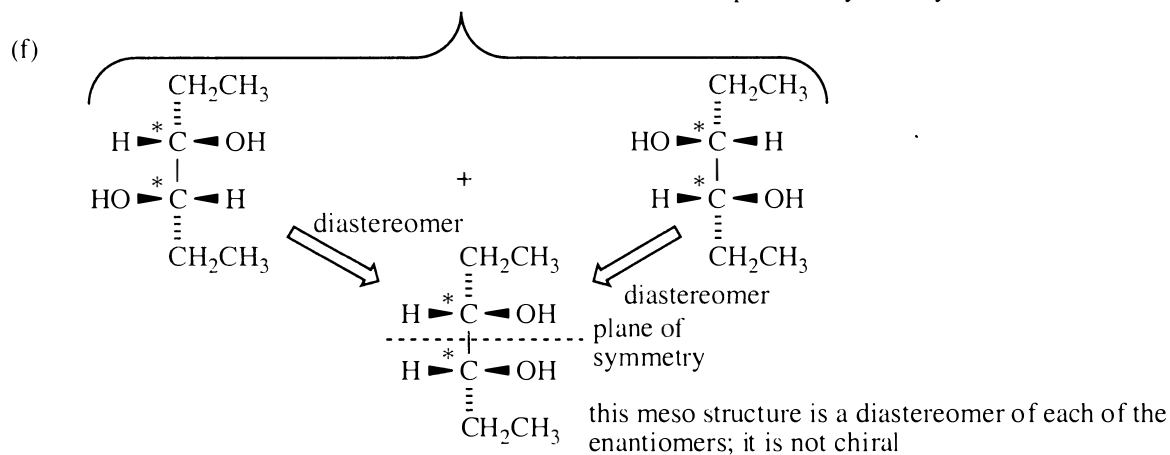
5-27



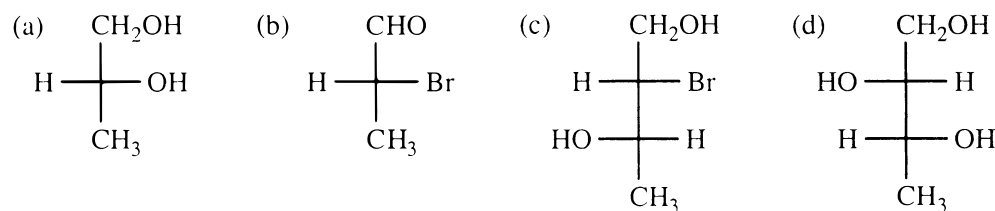
5-27 continued



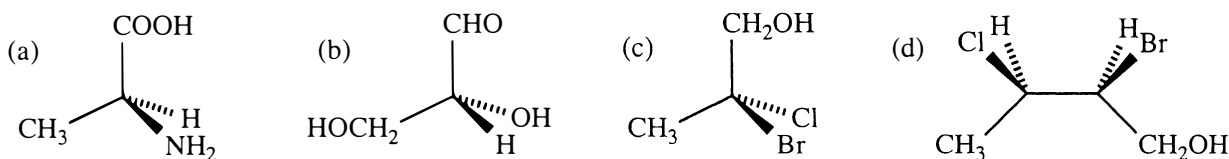
racemic mixture of enantiomers; each is chiral with no plane of symmetry



5-28



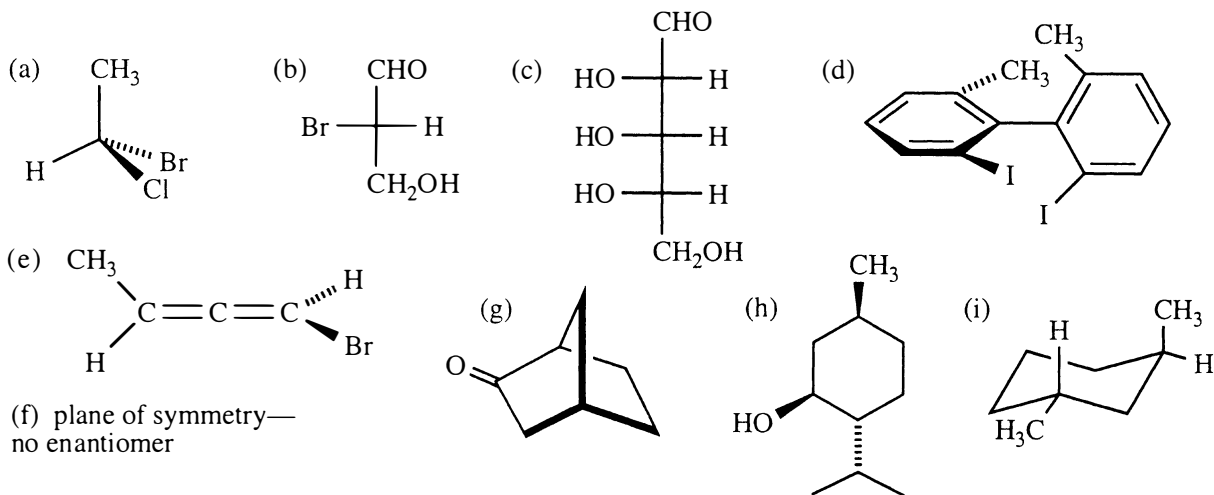
5-29 Your drawings may look different from these and still be correct. Check configuration by assigning *R* and *S* to be sure.



5-30

- (a) same (meso)—plane of symmetry, superimposable
 (b) enantiomers—configuration inverted at both asymmetric carbon atoms
 (c) enantiomers—configuration inverted at both asymmetric carbon atoms
 (d) enantiomers—solve this problem by switching two groups at a time to put the groups in the same positions as in the first structure; it takes three switches to make the identical compound, so they are enantiomers; an even number of switches would prove they are the same structure
 (e) enantiomers—configuration inverted at both asymmetric carbon atoms
 (f) diastereomers—configuration inverted at only one asymmetric carbon
 (g) enantiomers—configuration inverted at both asymmetric carbon atoms
 (h) same compound—rotate the right structure 180° around a horizontal axis and it becomes the left structure

5-31 Drawing the enantiomer of a chiral structure is as easy as drawing its mirror image.



5-32

- (a) $1.00 \text{ g} / 20.0 \text{ mL} = 0.050 \text{ g/mL}$; $20.0 \text{ cm} = 2.00 \text{ dm}$

$$[\alpha]_{\text{D}}^{25} = \frac{-1.25^\circ}{(0.0500)(2.00)} = -12.5^\circ$$

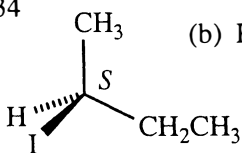
- (b) $0.050 \text{ g} / 2.0 \text{ mL} = 0.025 \text{ g/mL}$; $2.0 \text{ cm} = 0.20 \text{ dm}$

$$[\alpha]_{\text{D}}^{25} = \frac{+0.043^\circ}{(0.025)(0.20)} = +8.6^\circ$$

5-33 The 32% of the mixture that is (–)-tartaric acid will cancel the optical rotation of the 32% of the mixture that is (+)-tartaric acid, leaving only $(68 - 32) = 36\%$ of the mixture as excess (+)-tartaric acid to give measurable optical rotation. The specific rotation will therefore be only 36% of the rotation of pure (+)-tartaric acid: $(+12.0^\circ) \times 36\% = +4.3^\circ$

5-34

(a)

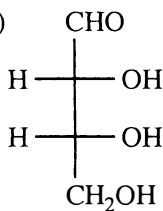
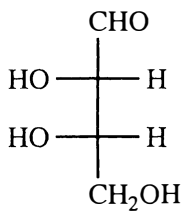
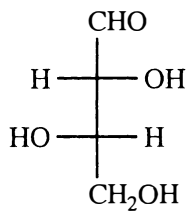
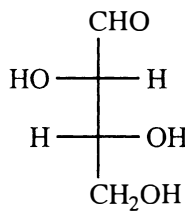
(b) Rotation of the enantiomer will be equal in magnitude, opposite in sign: -15.90° .(c) The rotation -7.95° is what percent of -15.90° ?

$$\frac{-7.95^\circ}{-15.90^\circ} \times 100\% = 50\% \text{ e.e.}$$

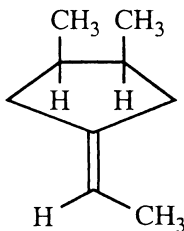
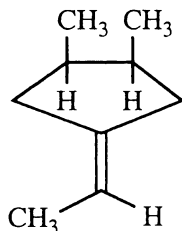
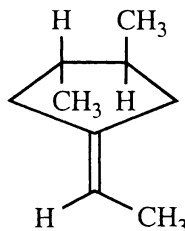
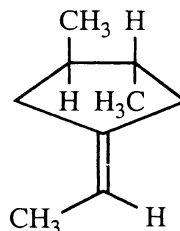
There is 50% excess of (*R*)-2-iodobutane over the racemic mixture; that is, another 25% must be *R* and 25% must be *S*. The total composition is 75% (*R*)-(-)-2-iodobutane and 25% (*S*)-(+)-2-iodobutane.

5-35 All structures in this problem are chiral.

(a)

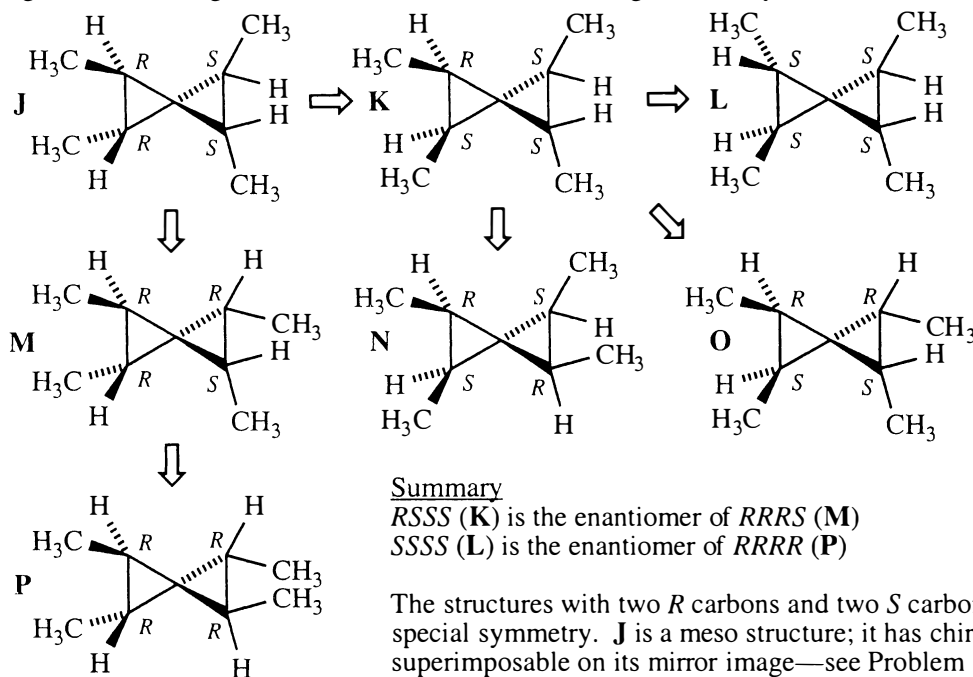
**A****B****C****D**enantiomers: **A** and **B**; **C** and **D**diastereomers: **A** and **C**; **A** and **D**; **B** and **C**; **B** and **D**

(b)

**E****F****G****H**enantiomers: **E** and **F**; **G** and **H**diastereomers: **E** and **G**; **E** and **H**; **F** and **G**; **F** and **H**

5-35 continued

(c) This structure is a challenge to visualize. A model helps. One way to approach this problem is to assign *R* and *S* configurations. Each arrow shows a change at one asymmetric carbon.



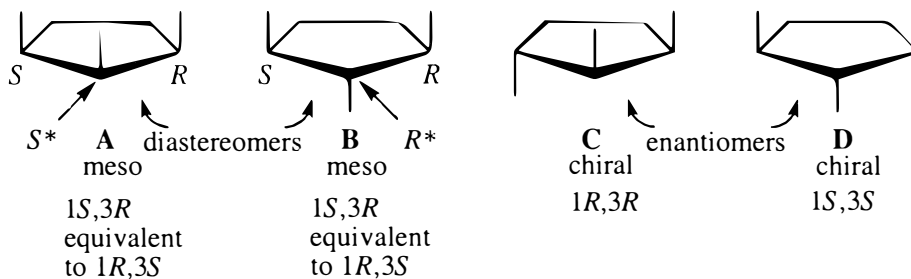
Summary

RSSS (**K**) is the enantiomer of *RRRS* (**M**)

SSSS (**L**) is the enantiomer of *RRRR* (**P**)

The structures with two *R* carbons and two *S* carbons (**J**, **N**, and **O**) have special symmetry. **J** is a meso structure; it has chirality centers and is superimposable on its mirror image—see Problem 5-20(h). **N** and **O** are enantiomers, and are diastereomers of all of the other structures. Give yourself a gold star if you got this correct!

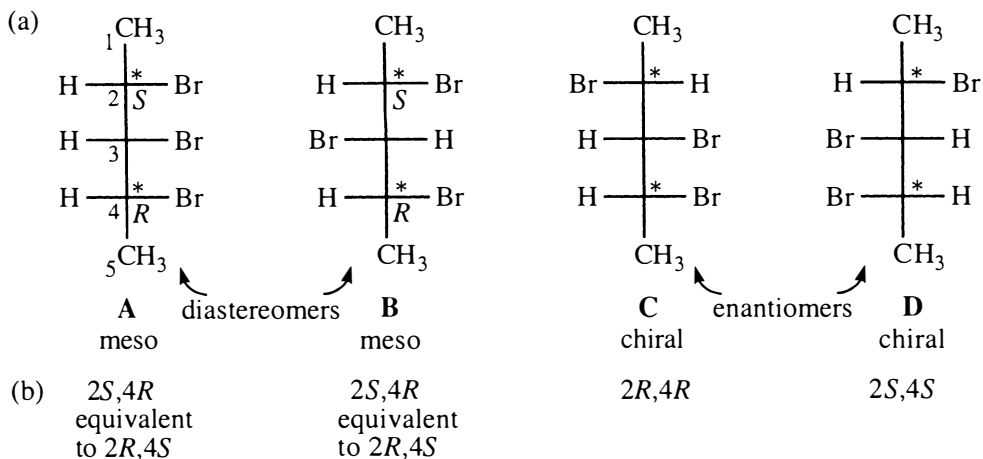
5-36



C and **D** are enantiomers. All other pairs are diastereomers.

*Structures **A** and **B** are both meso structures, but they are clearly different from each other. How can they be distinguished? One of the advanced rules of the Cahn-Ingold-Prelog system says: When two groups attached to an asymmetric carbon differ only in their absolute configuration, then the neighboring (*R*) stereocenter takes priority. Now the configuration of the central asymmetric carbon can be assigned: *S* for structure **A**, and *R* for structure **B**. This rule also applies to problem 5-37. (Thanks to Dr. Kantorowski for this explanation.)

5-37 This problem is similar to 5-36.

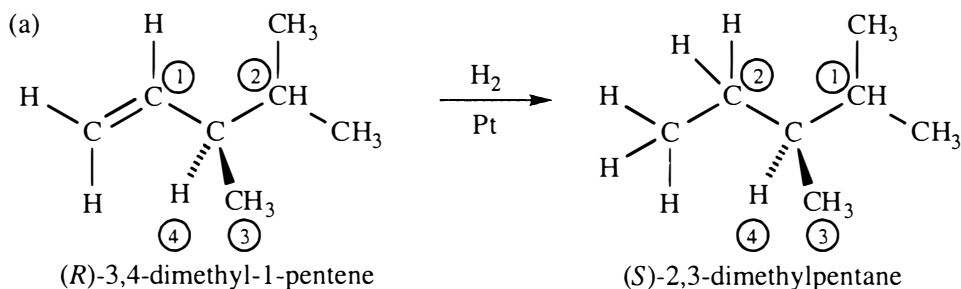


The configuration of carbon-3 in **A** and **B** can be assigned according to the rule described above in the solution to problem 5-36: C-3 in **A** is *S*, and C-3 in **B** is *R*.

(c) According to the IUPAC designation described in text Section 5-2B, a chirality center is "any atom holding a set of ligands in a spatial arrangement which is not superimposable on its mirror image." An asymmetric carbon must have four different groups on it, but in **A** and **B**, C-3 has two groups that are identical (except for their stereochemistry). C-3 holds its groups in a spatial arrangement that is superimposable on its mirror image, so it is not a chirality center. But it is stereogenic: in structure **A**, interchanging the H and Br at C-3 gives structure **B**, a diastereomer of **A**; therefore, C-3 is stereogenic.

(d) In structure **C** or **D**, C-3 is not stereogenic. Inverting the H and the Br, then rotating the structure 180° , shows that the same structure is formed. Therefore, interchanging two atoms at C-3 does *not* give a stereoisomer, so C-3 does not fit the definition of a stereogenic center.

5-38 The Cahn-Ingold-Prelog priorities of the groups are the circled numbers in (a).



(b) The reaction did not occur at the asymmetric carbon atom, so the configuration has not changed—the reaction went with retention of configuration at the asymmetric carbon.

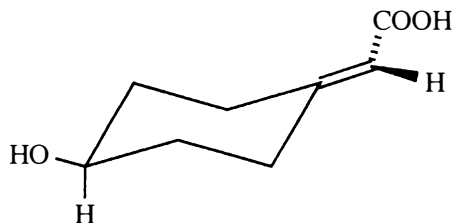
(c) The *name* changed because the *priority* of groups in the Cahn-Ingold-Prelog system of nomenclature changed. When the alkene became an ethyl group, its priority changed from the highest priority group to priority 2. (We will revisit this anomaly in problem 6-21(c).)

(d) There is no general correlation between *R* and *S* designation and the physical property of optical rotation. Professor Wade's poetic couplet makes an important point: do not confuse an object and its properties with the *name* for that object. (Scholars of Shakespeare have come to believe that this quote from Juliet is a veiled reference to designation of *R,S* configuration versus optical rotation of a chiral molecule. Shakespeare was *way* ahead of his time.)

5-39

(a) The product has no asymmetric carbon atoms but it has three stereocenters: the carbon with the OH, plus both carbons of the double bond. Interchange of two bonds on any of these makes the enantiomer.

(b) The product is an example of a chiral compound with no asymmetric carbons. Like the allenes, it is classified as an "extended tetrahedron"; that is, it has four groups that extend from the rigid molecule in four different directions. (A model will help.) In this structure, the plane containing the COOH and carbons of the double bond is perpendicular to the plane bisecting the OH and H and carbon that they are on. Since the compound is chiral, it is capable of being optically active.

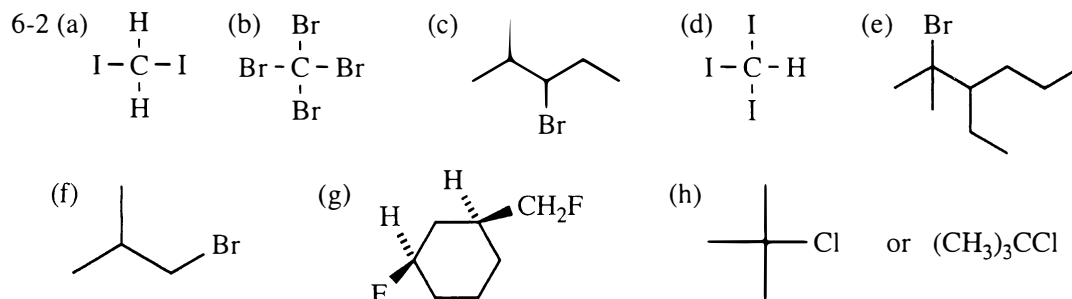


(c) As shown in text Figure 5-16, Section 5-6, catalytic hydrogenation that creates a new chirality center creates a racemic mixture (both enantiomers in a 1:1 ratio). A racemic mixture is not optically active. In contrast, by using a chiral enzyme to reduce the ketone to the alcohol (as in part (b)), an excess of one enantiomer was produced, so the product was optically active.

CHAPTER 6—ALKYL HALIDES: NUCLEOPHILIC SUBSTITUTION AND ELIMINATION

6-1 In problems like part (a), draw out the whole structure to detect double bonds.

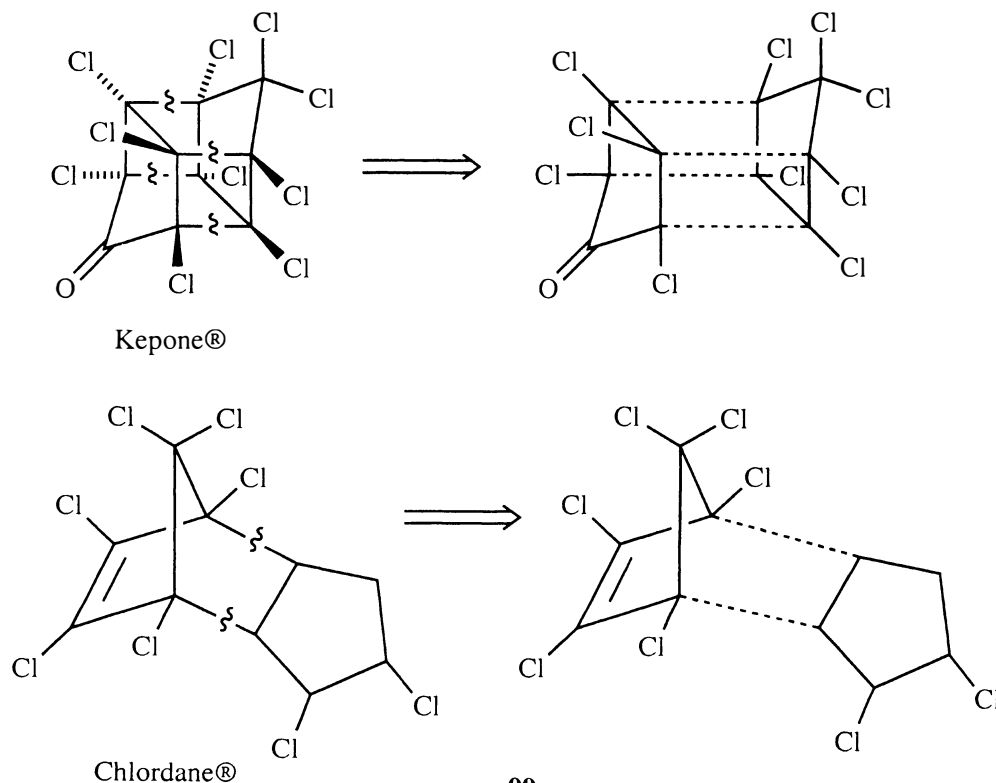
- (a) vinyl halide (c) aryl halide (e) vinyl halide
 (b) alkyl halide (d) alkyl halide (f) aryl halide



6-3 IUPAC name; common name; degree of halogen-bearing carbon

- (a) 1-chloro-2-methylpropane; isobutyl chloride; 1°
 (b) diiodomethane; methylene iodide; methyl
 (c) 1,1-dichloroethane; no common name; 1°
 (d) 2-bromo-1,1,1-trichloroethane; no common name; all 1°
 (e) trichloromethane; chloroform; methyl
 (f) 2-bromo-2-methylpropane; *t*-butyl bromide; 3°
 (g) 2-bromobutane; *sec*-butyl bromide; 2°
 (h) 1-chloro-2-methylbutane; no common name; 1°
 (i) *cis*-1-bromo-2-chlorocyclobutane; no common name; both 2°
 (j) 3-bromo-4-methylhexane; no common name; 2°
 (k) 4-fluoro-1,1-dimethylcyclohexane; no common name; 2°
 (l) *trans*-1,3-dichlorocyclopentane; no common name; all 2°

6-4



6-5 From the text, Section 2-9B, the bond dipole moment depends not only on bond length but also on charge separation, which in turn depends on the difference in electronegativities of the two atoms connected by the bond. Because chlorine's electronegativity (3.2) is significantly higher than iodine's (2.7), the C—Cl bond dipole is greater than that of C—I, despite C—I being a longer bond.

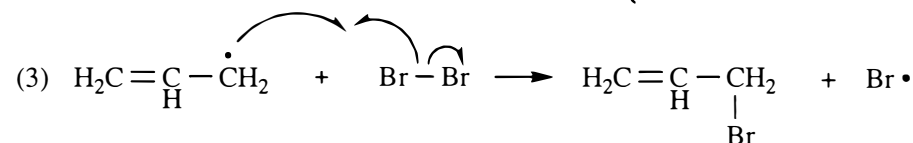
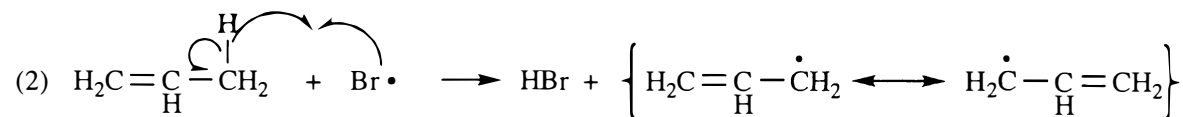
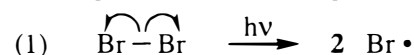
6-6

- (a) *n*-Butyl bromide has a higher molecular weight and less branching, and boils at a higher temperature than isopropyl bromide.
 (b) *t*-Butyl bromide has a higher molecular weight and a larger halogen, and despite its greater branching, boils at a higher temperature than isopropyl chloride.
 (c) *n*-Butyl bromide has a higher molecular weight and a larger halogen, and boils at a higher temperature than *n*-butyl chloride.

6-7 From Table 3-2, the density of hexane is 0.66; it will float on the water layer (d 1.00). From Table 6-2, the density of chloroform is 1.50; water will float on the chloroform. Water is immiscible with many organic compounds; whether water is the top layer or bottom layer depends on whether the other material is more dense or less dense than water. (This is an important consideration to remember in lab procedures.)

6-8

(a) Step (1) is initiation; steps (2) and (3) are propagation.



(b) Step (2): break allylic C—H, make H—Br: kJ/mole: + 364 – (+ 368) = – 4 kJ/mole

kcal/mole: + 87 – (+ 88) = – 1 kcal/mole

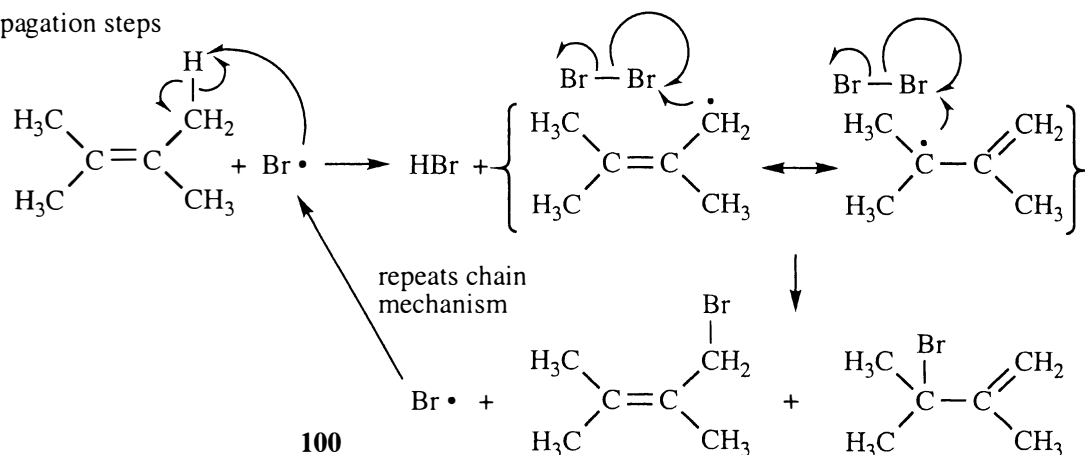
Step (3): break Br—Br, make allylic C—Br: kJ/mole: + 192 – (+ 280) = – 88 kJ/mole

kcal/mole: + 46 – (+ 67) = – 21 kcal/mole

ΔH overall = – 4 + – 88 = – 92 kJ/mole (– 1 + – 21 = – 22 kcal/mole)

This is a very exothermic reaction; it is reasonable to expect a small activation energy in step (1), so this reaction should be very rapid.

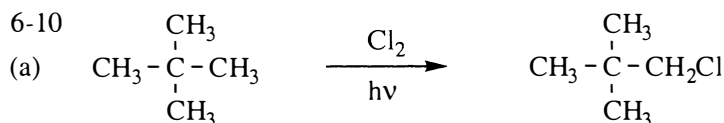
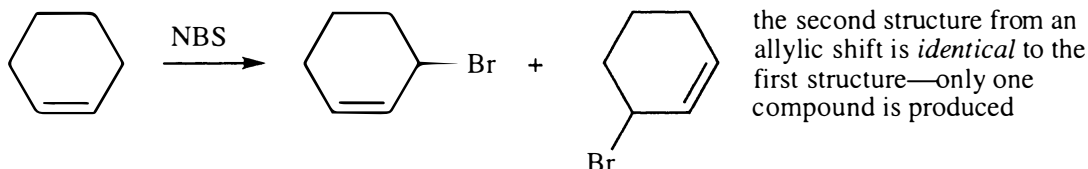
6-9 (a) propagation steps



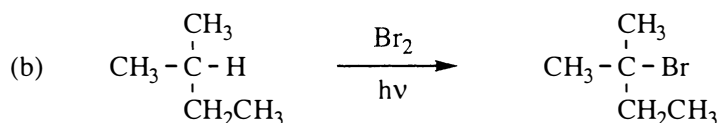
6-9 continued

The resonance-stabilized allylic radical intermediate has radical character on both the 1° and 3° carbons, so bromine can bond to either of these carbons producing two isomeric products.

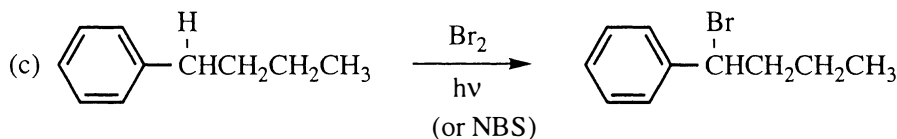
(b) Allylic bromination of cyclohexene gives 3-bromocyclohex-1-ene regardless of whether there is an allylic shift. Either pathway leads to the same product. If one of the ring carbons were somehow marked or labeled, then the two products can be distinguished. (We will see in following chapters how labeling is done experimentally.)



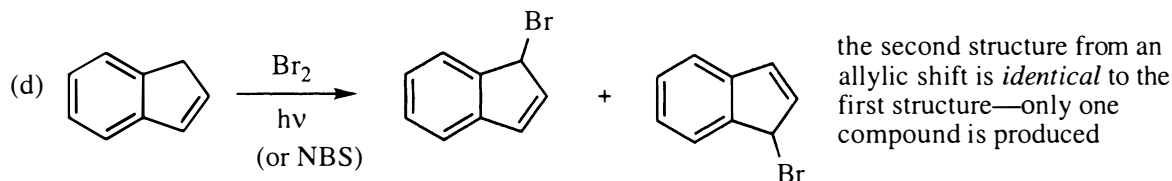
This compound has only one type of hydrogen—only one monochlorine isomer can be produced.



Bromination has a strong preference for abstracting hydrogens (like 3°) that give stable radical intermediates.



Bromine atom will abstract the hydrogen giving the most stable radical; in this case, the radical intermediate will be stabilized by resonance with the benzene ring.

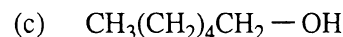
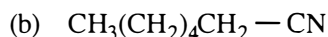


Bromine atom will abstract the hydrogen giving the most stable radical; in this case, the radical intermediate will be stabilized by resonance with the benzene ring.

6-11

- (a) substitution—Br is replaced
- (b) elimination—H and OH are lost
- (c) elimination—both Br atoms are lost

6-12



6-13 The rate law is first order in both 1-bromobutane, C_4H_9Br , and methoxide ion. If the concentration of C_4H_9Br is lowered to one-fifth the original value, the rate must decrease to one-fifth; if the concentration of methoxide is doubled, the rate must also double. Thus, the rate must decrease to 0.02 mole/L per second:

$$\text{rate} = \underbrace{(0.05 \text{ mole/L per second})}_{\text{original rate}} \times \underbrace{\frac{(0.1 \text{ M})}{(0.5 \text{ M})}}_{\text{change in } C_4H_9Br} \times \underbrace{\frac{(2.0 \text{ M})}{(1.0 \text{ M})}}_{\text{change in } NaOCH_3} = \underbrace{0.02 \text{ mole/L per second}}_{\text{new rate}}$$

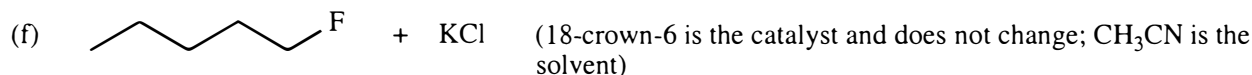
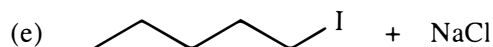
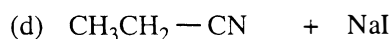
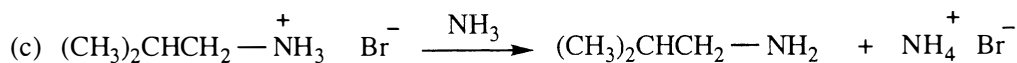
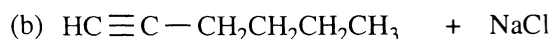
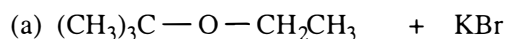
A completely different way to answer this problem is to solve for the rate constant k , then put in new values for the concentrations.

$$\text{rate} = k [C_4H_9Br] [NaOCH_3] \implies 0.05 \text{ mole L}^{-1} \text{ sec}^{-1} = k (0.5 \text{ mol L}^{-1}) (1.0 \text{ mol L}^{-1}) \implies$$

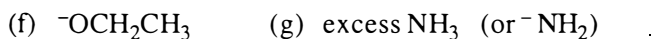
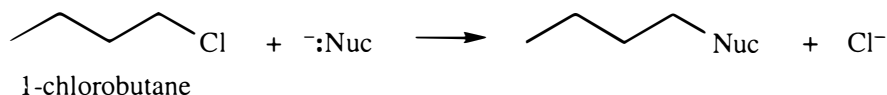
$$\text{rate constant } k = 0.1 \text{ L mol}^{-1} \text{ sec}^{-1}$$

$$\text{rate} = k [CH_3I] [NaOH] = (0.1 \text{ L mol}^{-1} \text{ sec}^{-1}) (0.1 \text{ mol L}^{-1}) (2.0 \text{ mol L}^{-1}) = 0.02 \text{ mole L}^{-1} \text{ sec}^{-1}$$

6-14 Organic and inorganic products are shown here for completeness.



6-15 All reactions in this problem follow the same pattern; the only difference is the nucleophile (^-Nuc). Only the nucleophile is listed below. (Cations like Na^+ or K^+ accompany the nucleophile but are simply spectator ions and do not take part in the reaction; they are not shown here.)



6-16

(a) $(CH_3CH_2)_2NH$ is a better nucleophile—less hindered

(b) $(CH_3)_2S$ is a better nucleophile—S is larger, more polarizable than O

(c) PH_3 is a better nucleophile—P is larger, more polarizable than N

(d) CH_3S^- is a better nucleophile—anions are better than neutral atoms of the same element

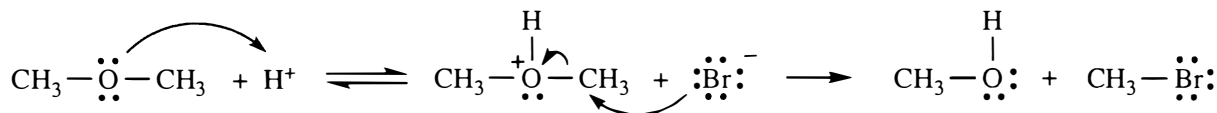
(e) $(CH_3)_3N$ is a better nucleophile—less electronegative than oxygen, better able to donate an electron pair

(f) CH_3S^- is a better nucleophile—anions are generally better than neutral atoms, and S is larger and more polarizable than O

(g) $CH_3CH_2CH_2O^-$ is a better nucleophile—less branching, less steric hindrance

(h) I^- is a better nucleophile—larger, more polarizable

6-17 A mechanism must show *electron movement*.



Protonation converts OCH_3 to a good leaving group.

6-18 The type of carbon with the halide, and relative leaving group ability of the halide, determine the reactivity.

methyl iodide > methyl chloride > ethyl chloride > isopropyl bromide >> neopentyl bromide, t -butyl iodide $\left. \vphantom{\begin{array}{l} \text{methyl iodide} \\ \text{methyl chloride} \\ \text{ethyl chloride} \\ \text{isopropyl bromide} \end{array}} \right\} \begin{array}{l} \text{least} \\ \text{reactive} \end{array}$

Predicting the relative order of neopentyl bromide and t -butyl iodide would be difficult because both would be extremely slow.

6-19 In all cases, the less hindered structure is the better $\text{S}_{\text{N}}2$ substrate.

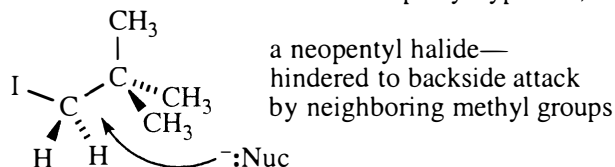
(a) 2-methyl-1-iodopropane (1° versus 3°)

(b) cyclohexyl bromide (2° versus 3°)

(c) isopropyl bromide (no substituent on neighboring carbon)

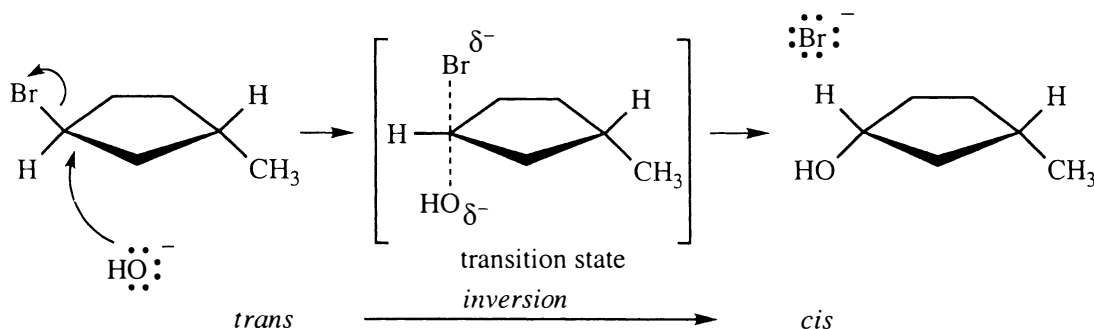
(d) 2-chlorobutane (even though this is a 2° halide, it is easier to attack than the 1° neopentyl type in 2,2-dimethyl-1-chlorobutane—see below)

(e) isopropyl iodide (same reason as in (d))

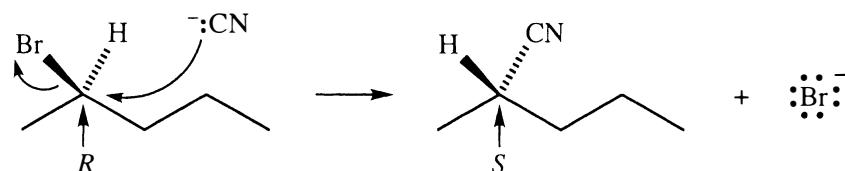


6-20 All $\text{S}_{\text{N}}2$ reactions occur with inversion of configuration at carbon.

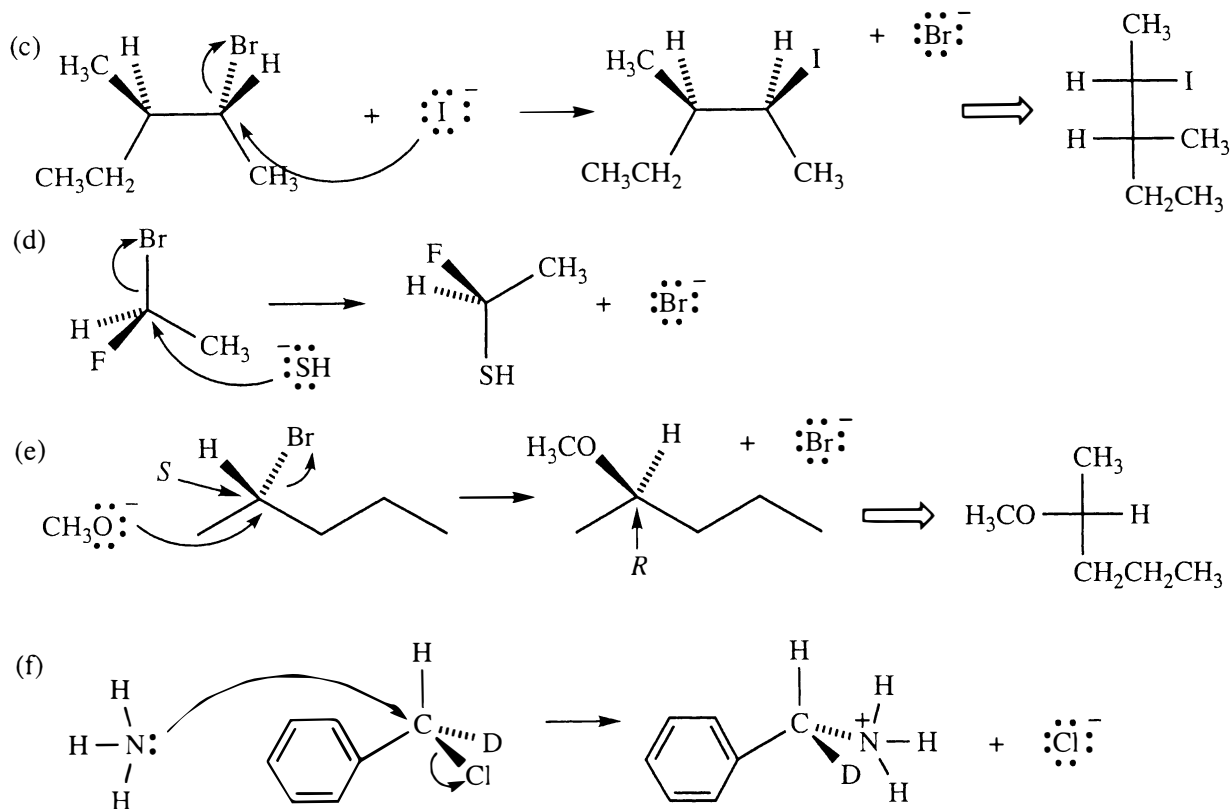
(a)



(b)

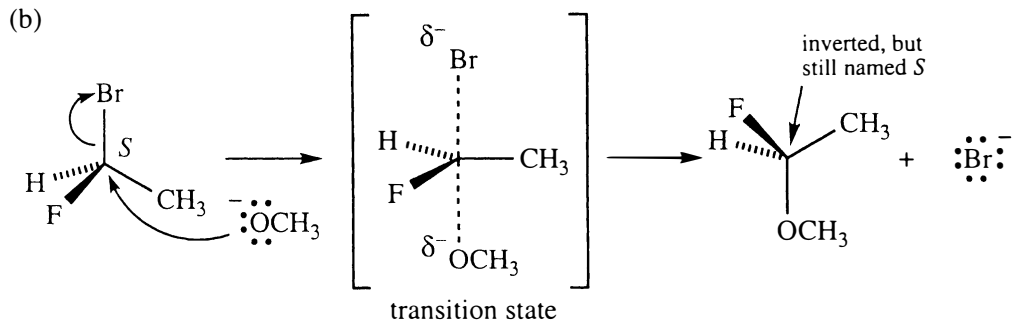


6-20 continued



6-21

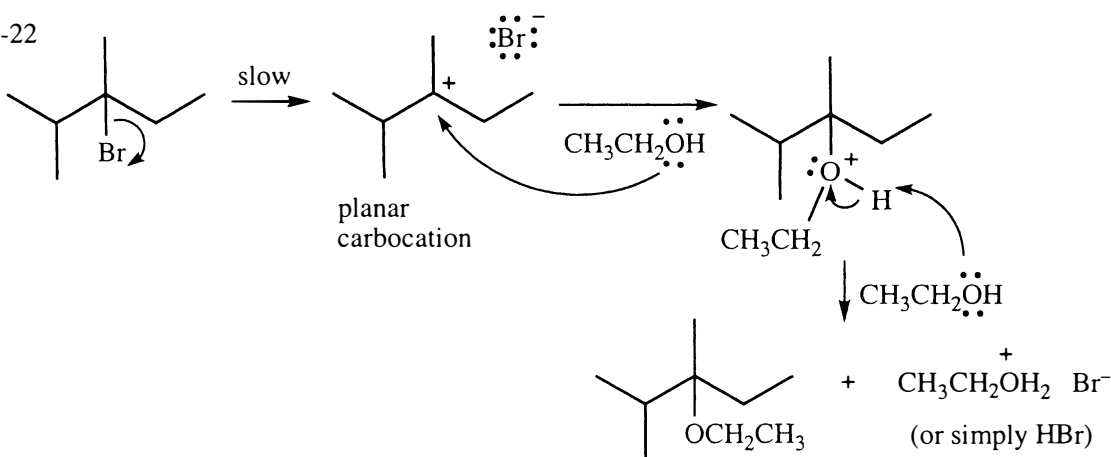
(a) The best leaving groups are the weakest bases. Bromide ion is so weak it is not considered at all basic; it is an excellent leaving group. Fluoride is moderately basic, by far the most basic of the halides. It is a terrible leaving group. Bromide is many orders of magnitude better than fluoride in leaving group ability.



(c) As noted on the structure above, the configuration is inverted even though the designations of the configuration for both the starting material and the product are *S*; the oxygen of the product has a lower priority than the bromine it replaces. Refer to the solution to problem 5-38, p. 97, for the caution about confusing absolute configuration with the *designation* of configuration.

(d) The result is perfectly consistent with the S_N2 mechanism. Even though both the reactant and the product have the *S* designation, the configuration has been inverted: the nomenclature priority of fluorine changes from second (after bromine) in the reactant to first (before oxygen) in the product. While the designation may be misleading, the structure shows with certainty that an inversion has occurred.

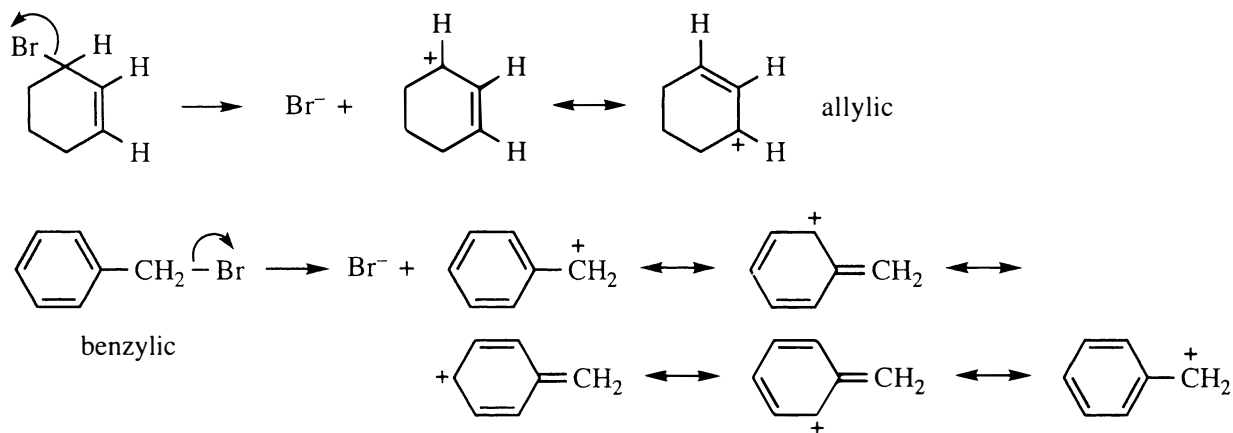
6-22



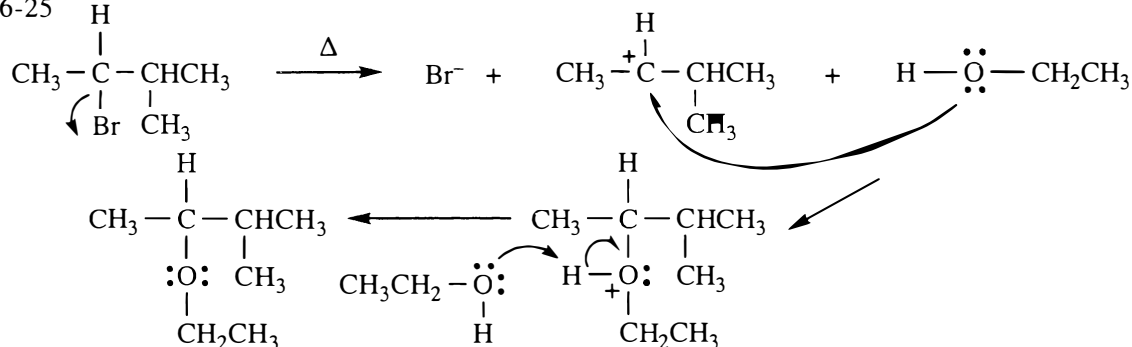
6-23 The structure that can form the more stable carbocation will undergo $\text{S}_{\text{N}}1$ faster.

- (a) 2-bromopropane: will form a 2° carbocation
- (b) 2-bromo-2-methylbutane: will form a 3° carbocation
- (c) allyl bromide is faster than *n*-propyl bromide: allyl bromide can form a resonance-stabilized intermediate.
- (d) 2-bromopropane: will form a 2° carbocation
- (e) 2-iodo-2-methylbutane is faster than *t*-butyl chloride (iodide is a better leaving group than chloride)
- (f) 2-bromo-2-methylbutane (3°) is faster than ethyl iodide (1°); although iodide is a somewhat better leaving group, the difference between 3° and 1° carbocation stability dominates

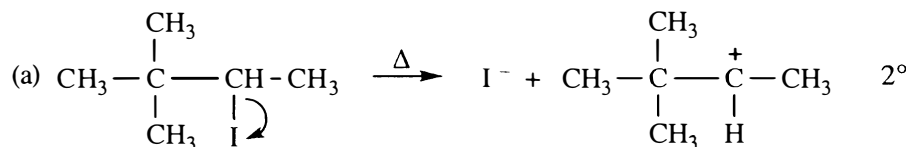
6-24 Ionization is the rate-determining step in $\text{S}_{\text{N}}1$. Anything that stabilizes the intermediate will speed the reaction. Both of these compounds form resonance-stabilized intermediates.



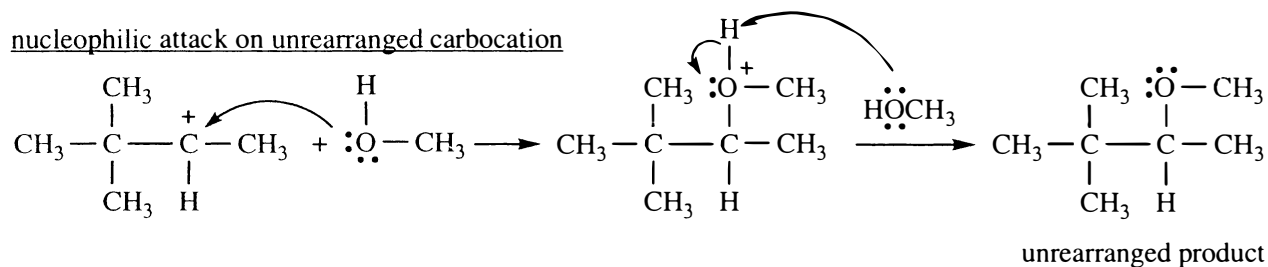
6-25



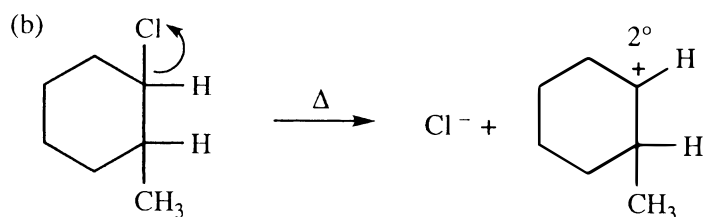
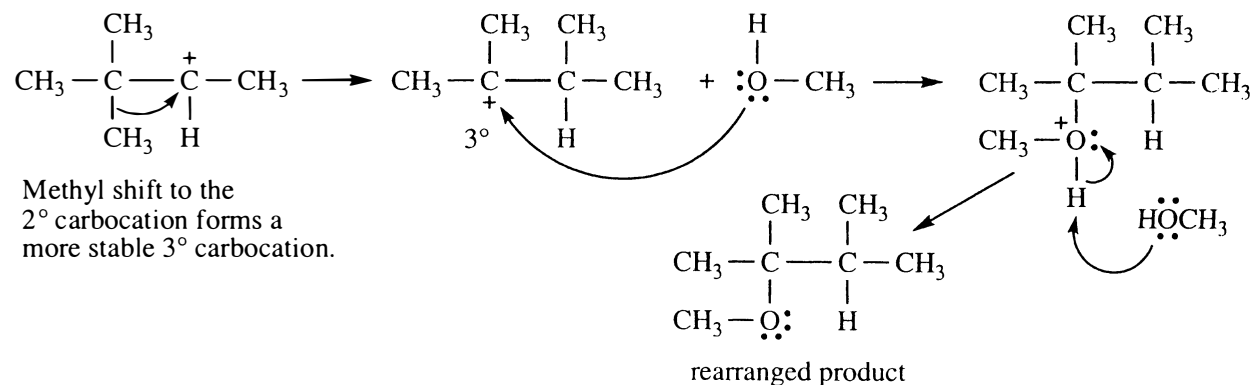
6-26 It is important to analyze the structure of carbocations to consider if migration of any groups from adjacent carbons will lead to a more stable carbocation. As a general rule, if rearrangement would lead to a more stable carbocation, a carbocation will rearrange. (Beginning with this problem, only those unshared electrons involved in a particular step will be shown.)



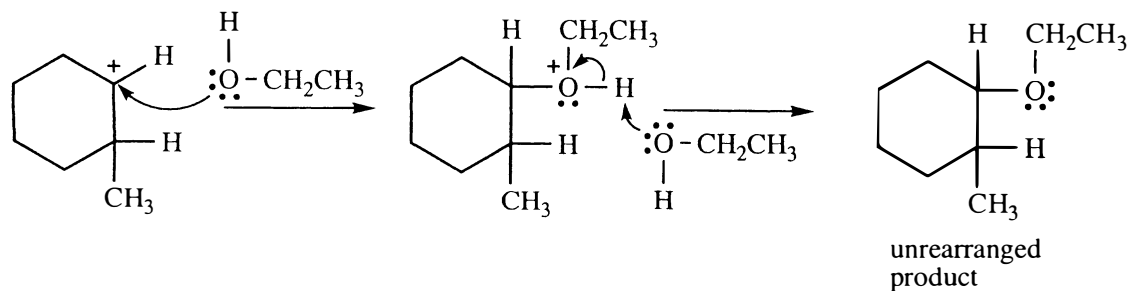
nucleophilic attack on unrearranged carbocation



nucleophilic attack after carbocation rearrangement

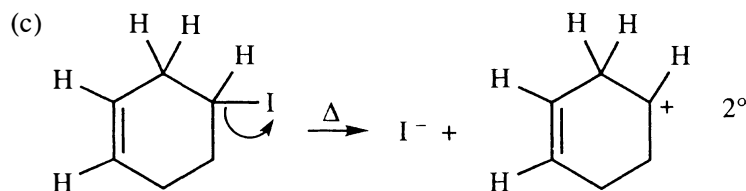
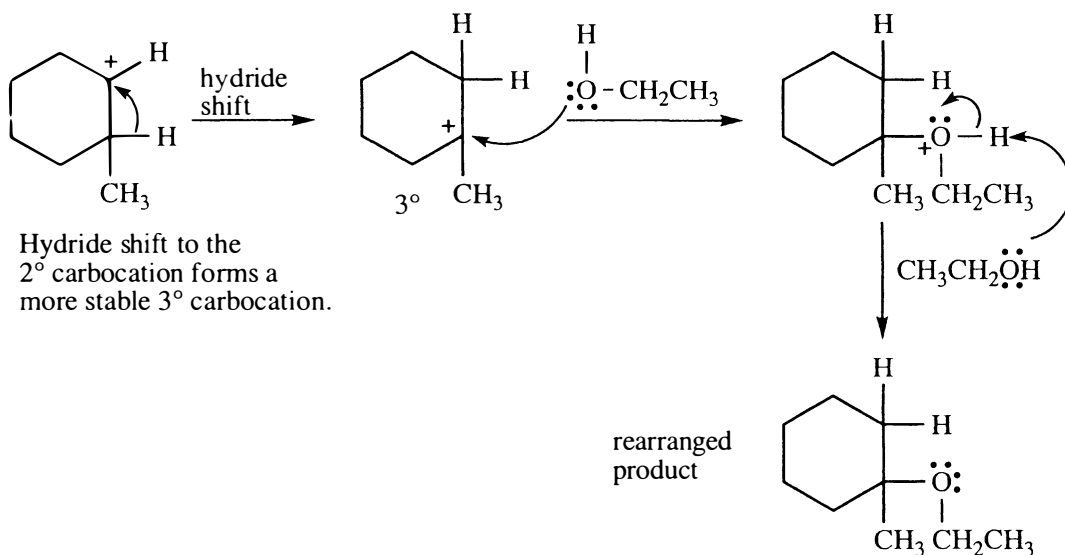


nucleophilic attack on unrearranged carbocation



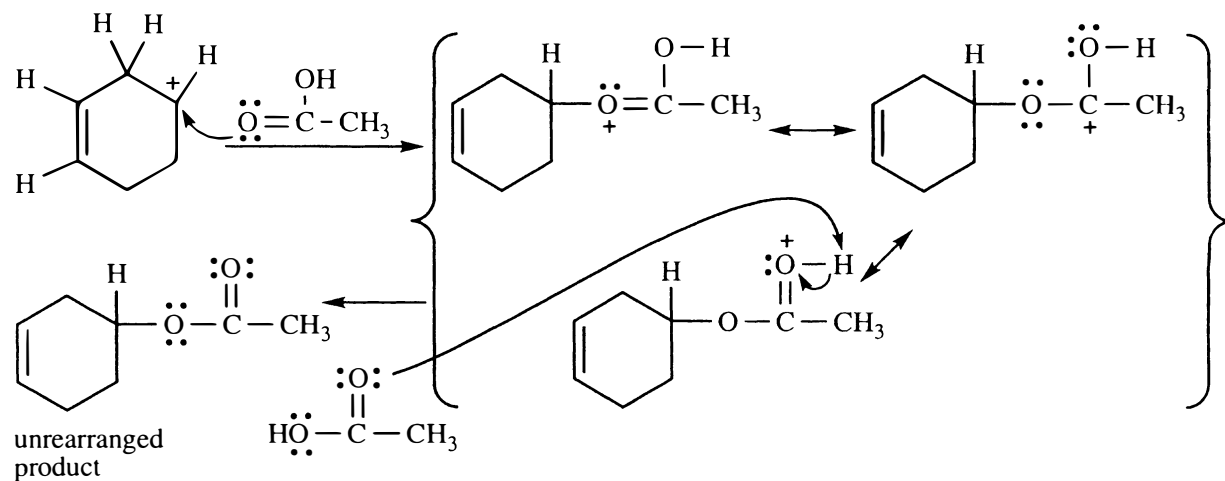
6-26(b) continued

nucleophilic attack after carbocation rearrangement



Note: braces are used to indicate the ONE chemical species represented by multiple resonance forms.

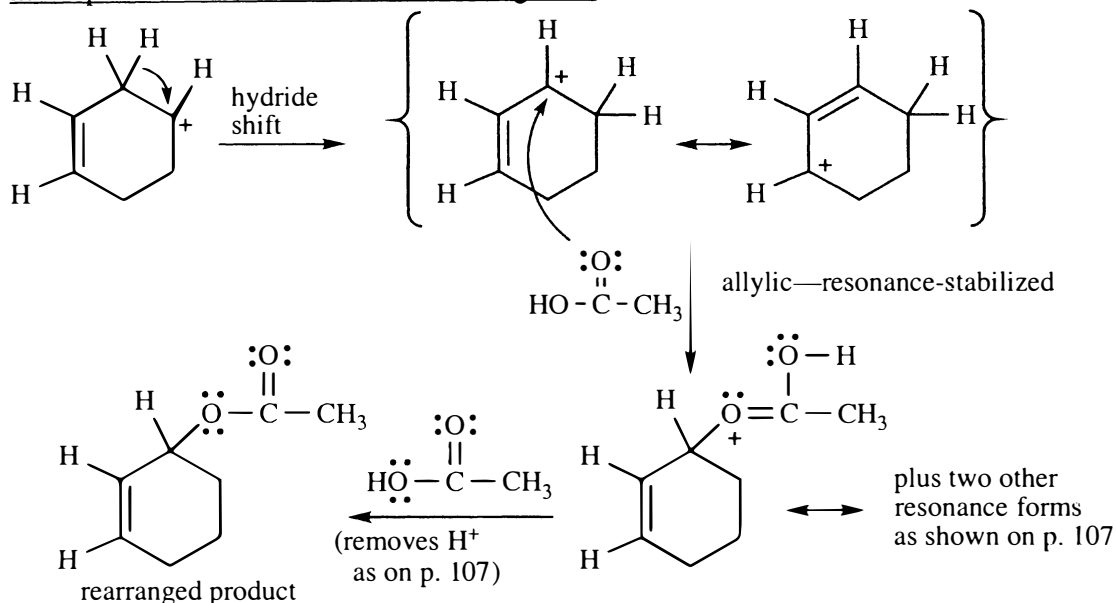
nucleophilic attack on unrearranged carbocation



The most basic species in a mixture is the most likely to remove a proton. In this reaction, acetic acid is more basic than iodide ion.

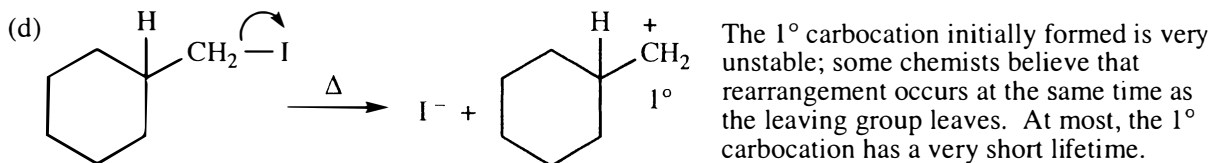
6-26(c) continued

nucleophilic attack after carbocation rearrangement

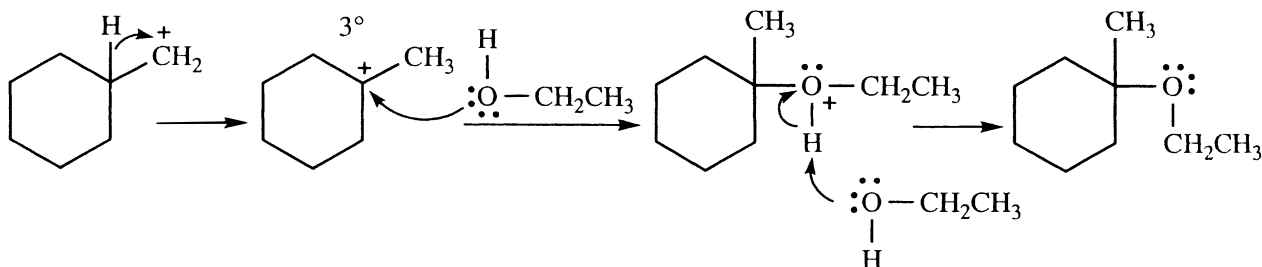


Comments on 6-26(c)

- (1) The hydride shift to a 2° carbocation generates an allylic, resonance-stabilized 2° carbocation.
- (2) The double-bonded oxygen of acetic acid is more nucleophilic because of the resonance forms it can have after attack. (See Solved Problem 1-5 and Problem 1-16 in the text.)
- (3) Attack on only one carbon of the allylic carbocation is shown. In reality, both positive carbons would be attacked in equal amounts, but they would give the identical product *in this case*. In other compounds, however, attack on the different carbons might give different products. **ALWAYS CONSIDER ALL POSSIBILITIES.**

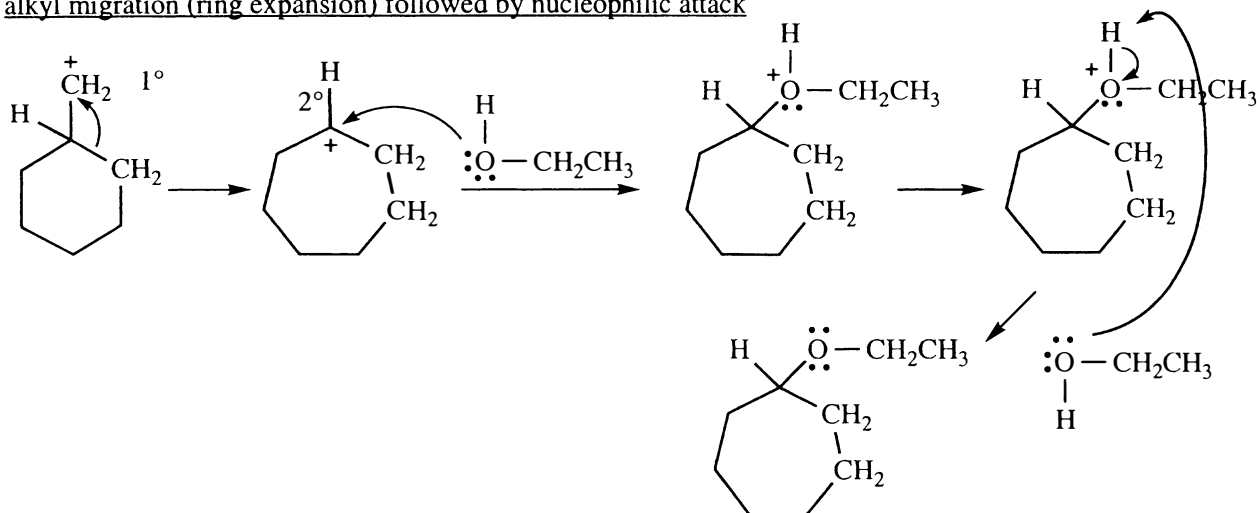


hydride shift followed by nucleophilic attack

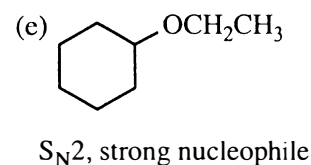
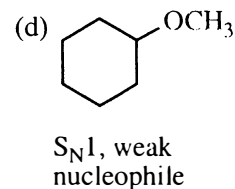
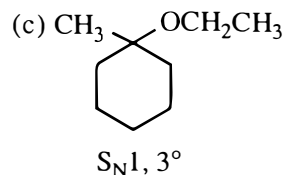
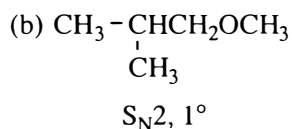
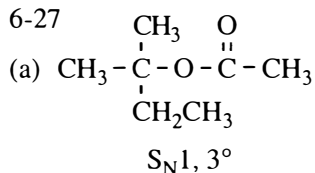


6-26 (d) continued

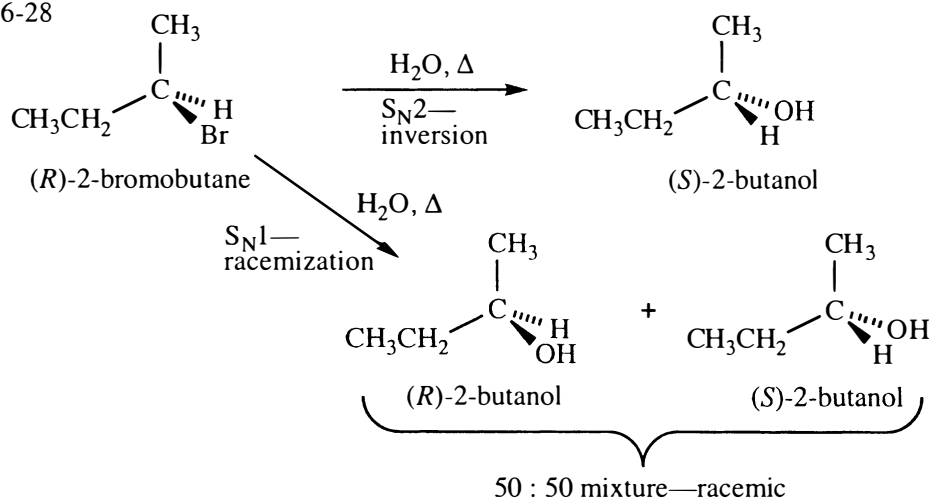
alkyl migration (ring expansion) followed by nucleophilic attack



6-27



6-28

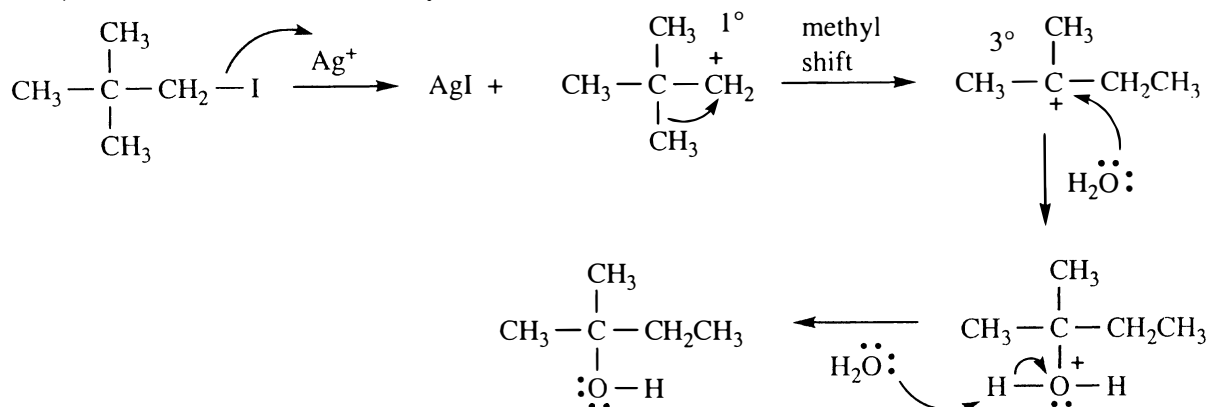


If $\text{S}_{\text{N}}1$, which gives racemization, occurs exactly twice as fast as $\text{S}_{\text{N}}2$, which gives inversion, then the racemic mixture (50 : 50 $R + S$) is 66.7% of the mixture and the rest, 33.3%, is the S enantiomer from $\text{S}_{\text{N}}2$. Therefore, the excess of one enantiomer over the racemic mixture must be 33.3%, the enantiomeric excess. (In the racemic mixture, the R and S "cancel" each other algebraically as well as in optical rotation.)

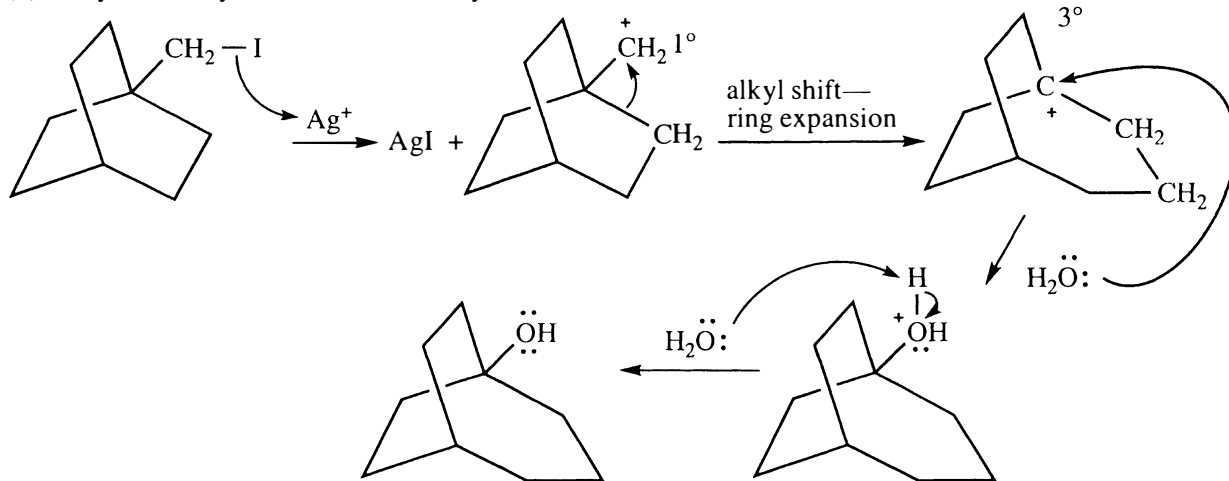
The optical rotation of pure (S)-2-butanol is $+13.5^\circ$. The optical rotation of this mixture is:
 $33.3\% \times +13.5^\circ = +4.5^\circ$

6-29

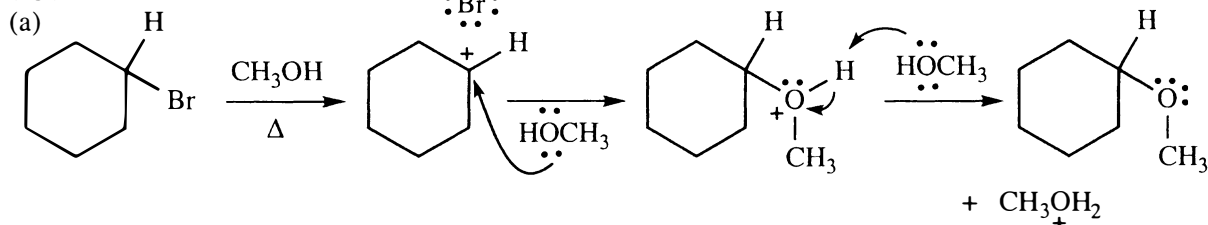
(a) Methyl shift may occur simultaneously with ionization. The lifetime of 1° carbocations is exceedingly short; some chemists believe that they are only a transition state to the rearranged product.



(b) Alkyl shift may occur simultaneously with ionization.



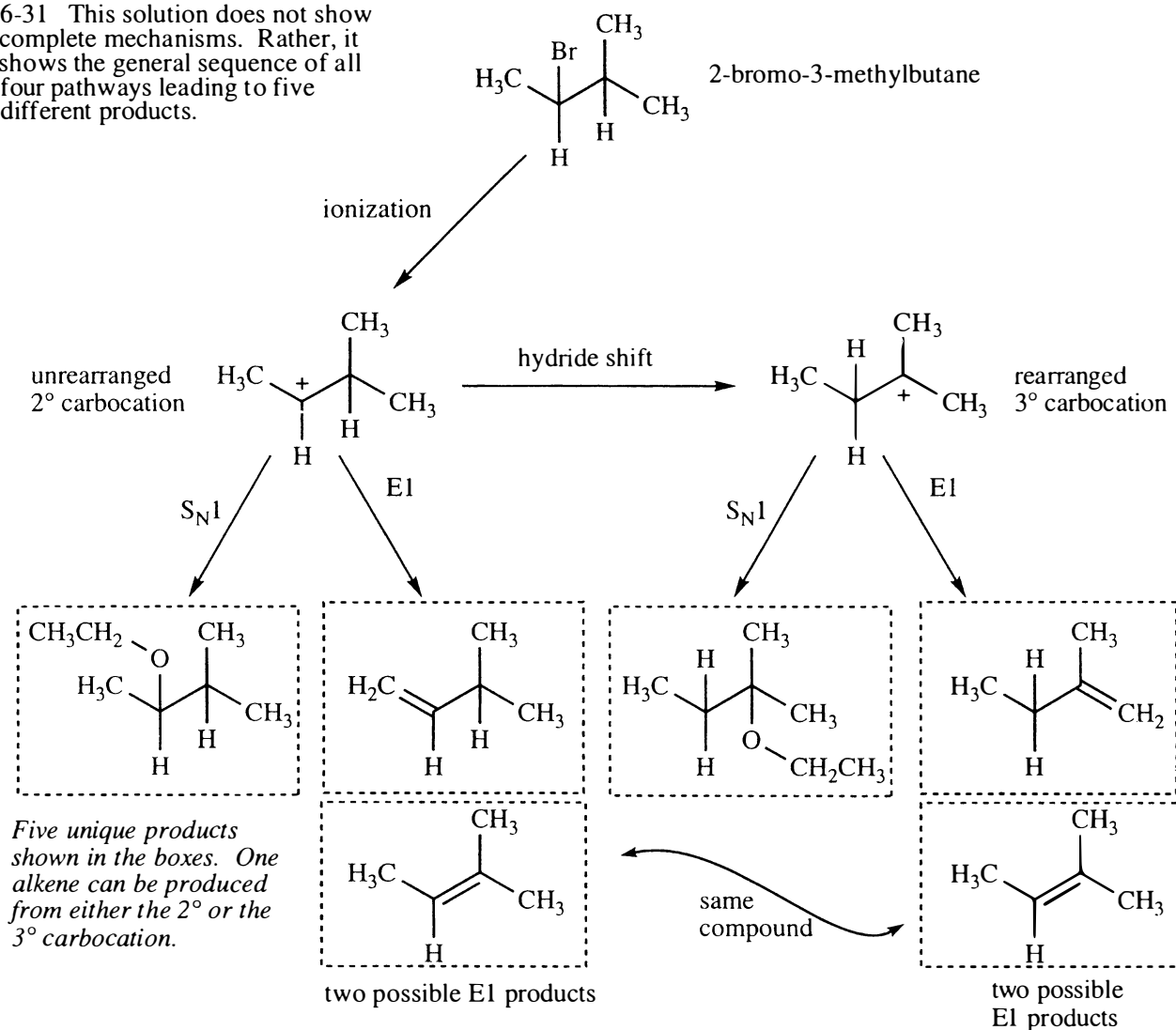
6-30



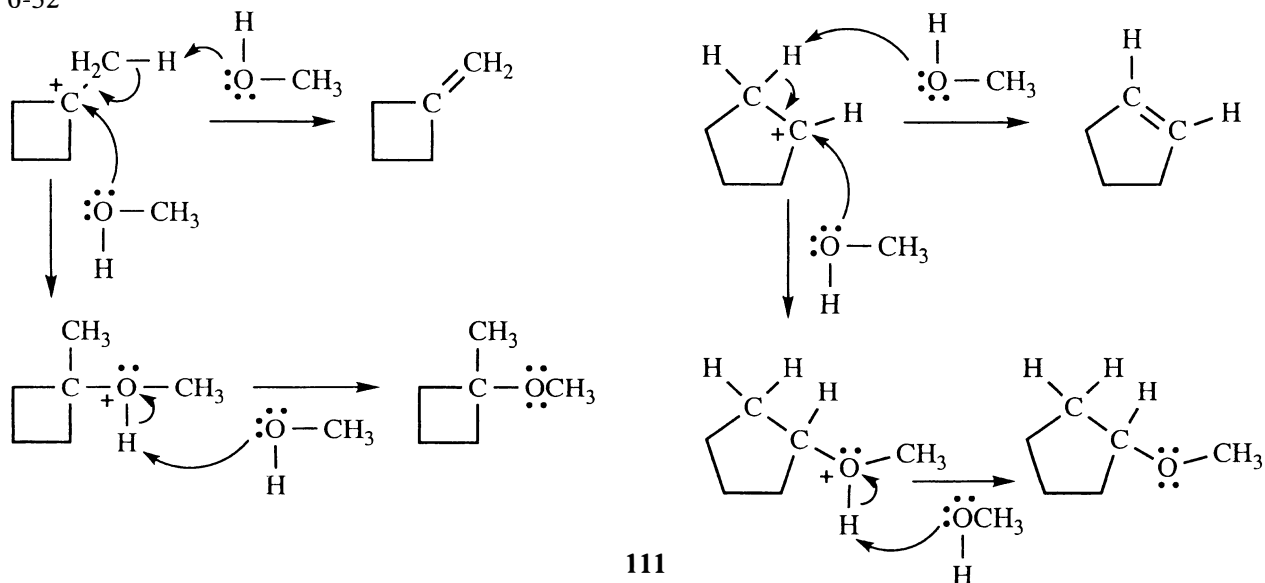
The $\text{S}_{\text{N}}1$ mechanism begins with ionization to form a carbocation, attack of a nucleophile, and in the case of ROH nucleophiles, removal of a proton by a base to form a neutral product.

(b) In the $\text{E}1$ reaction, the solvent (methanol, in this case) serves two functions: it aids the ionization process by solvating both the leaving group (bromide) and the carbocation; and second, it serves as a base to remove the proton from a carbon adjacent to the carbocation in order to form the carbon-carbon double bond. The $\text{S}_{\text{N}}1$ mechanism adds a third function to the solvent: the first step is the same as in $\text{E}1$, ionization to form the carbocation; the second step has the solvent acting as a nucleophile—this step is different from $\text{E}1$; third, the solvent acts like a base and removes a proton, although from an oxygen ($\text{S}_{\text{N}}1$) and not a carbon ($\text{E}1$). Solvents are versatile!

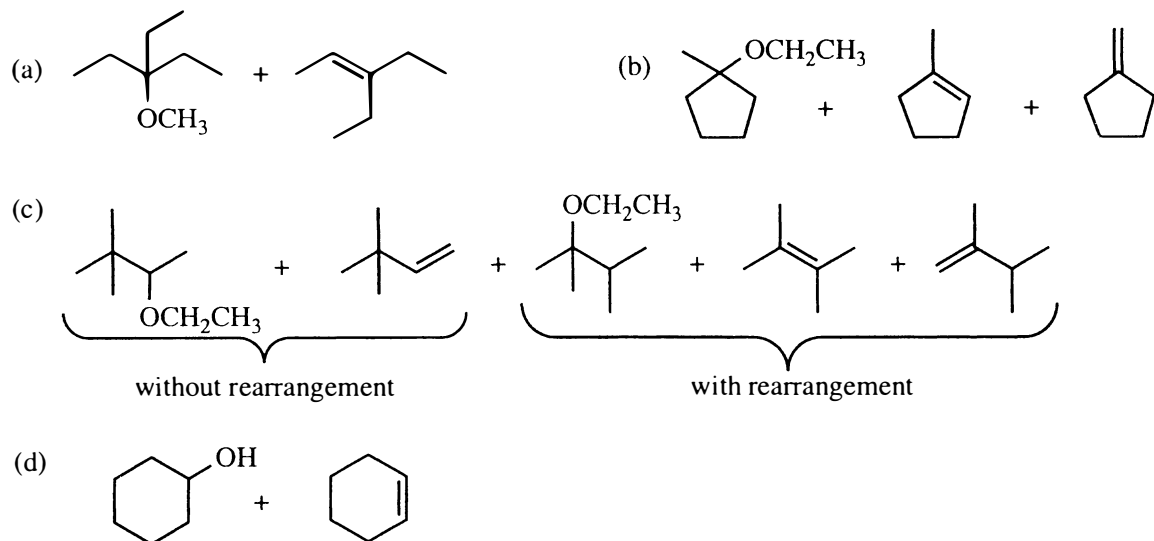
6-31 This solution does not show complete mechanisms. Rather, it shows the general sequence of all four pathways leading to five different products.



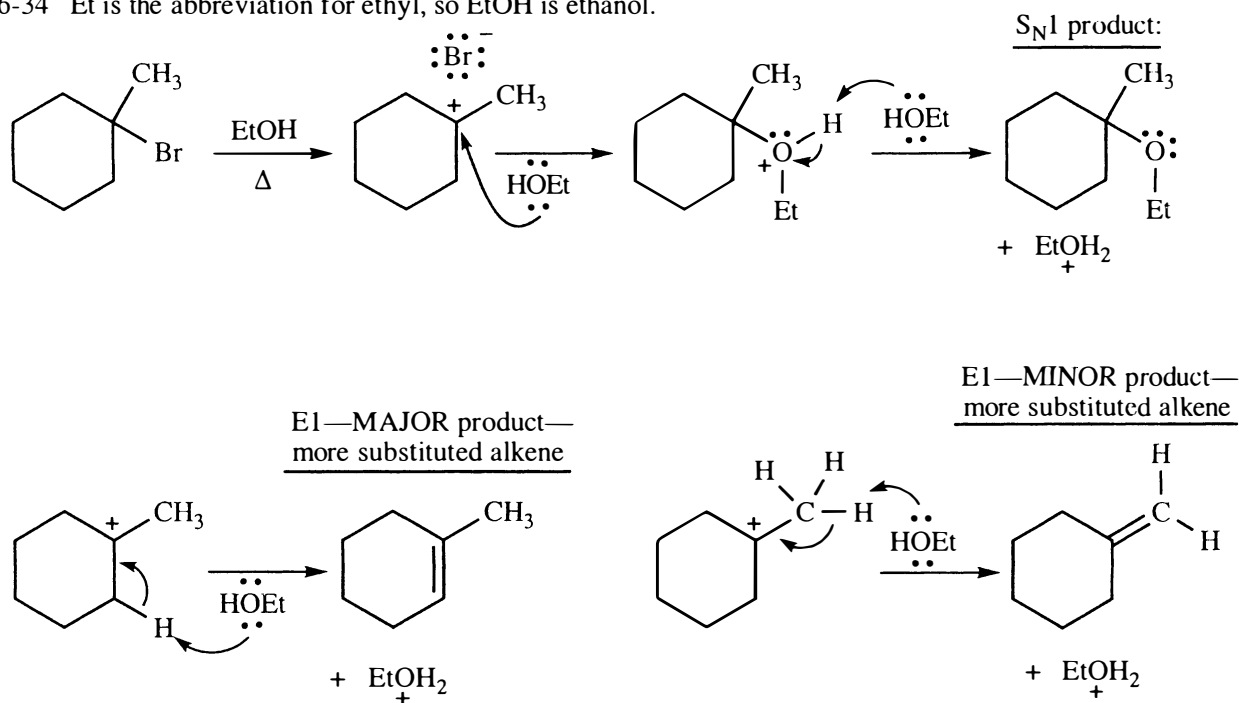
6-32



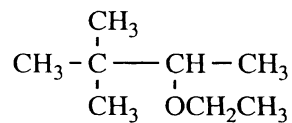
6-33 Substitution products are shown first, then elimination products.



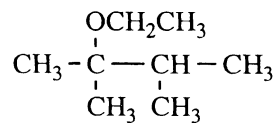
6-34 Et is the abbreviation for ethyl, so EtOH is ethanol.



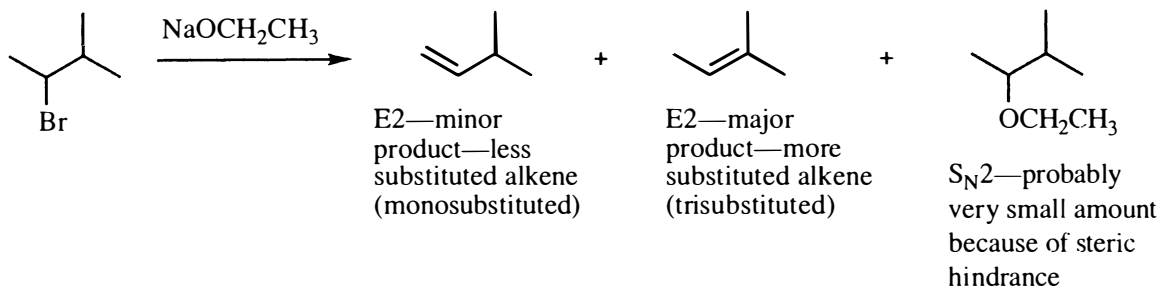
6-35 without rearrangement



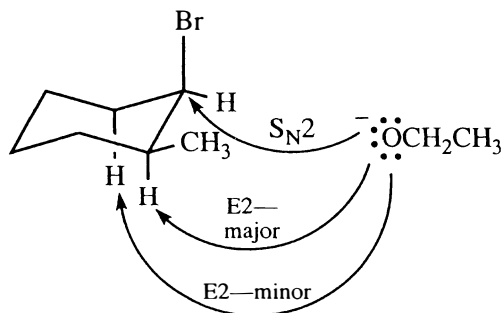
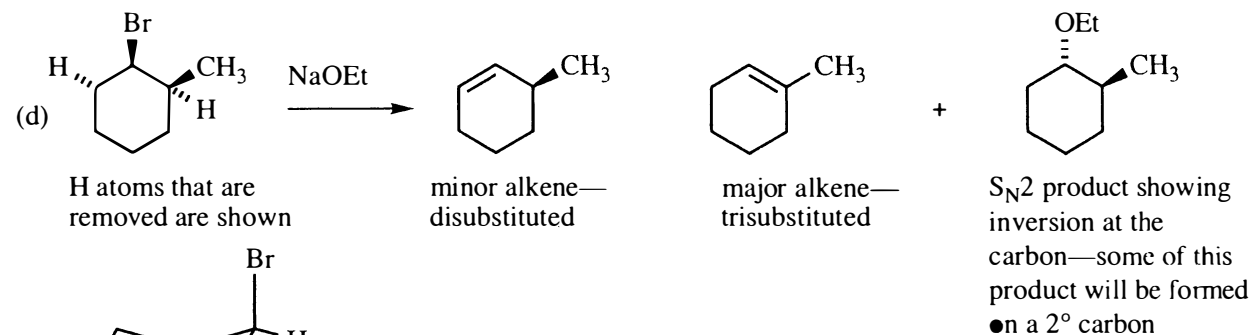
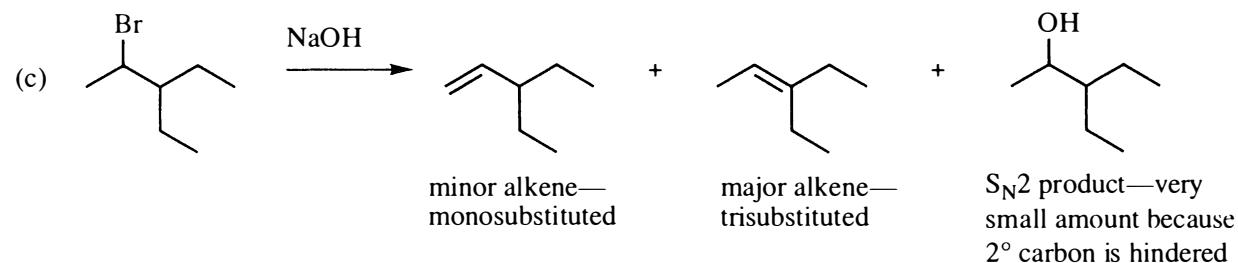
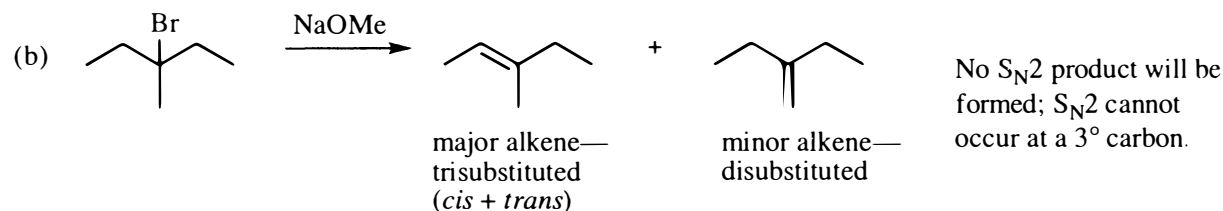
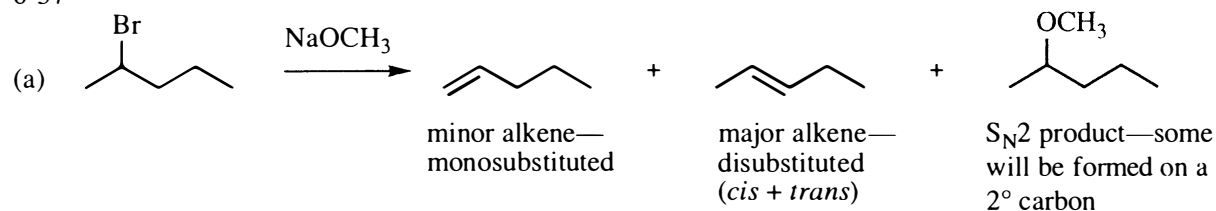
with rearrangement



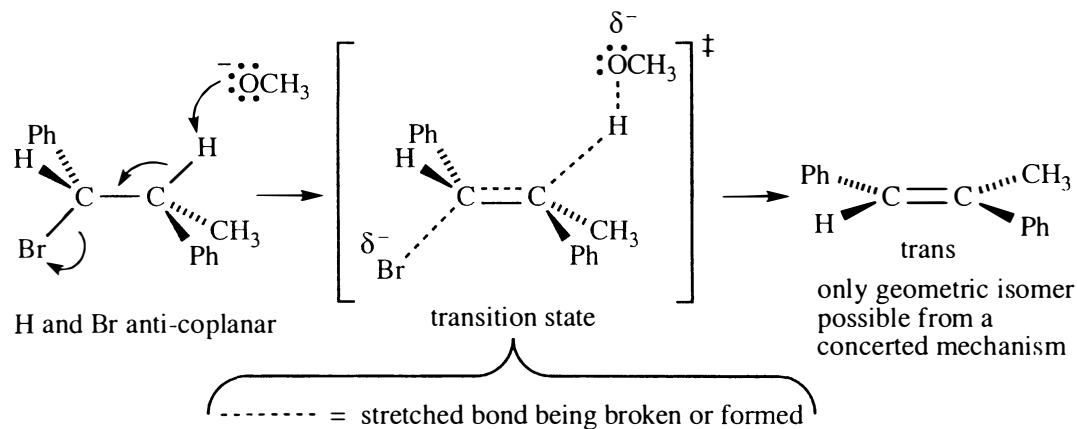
6-36



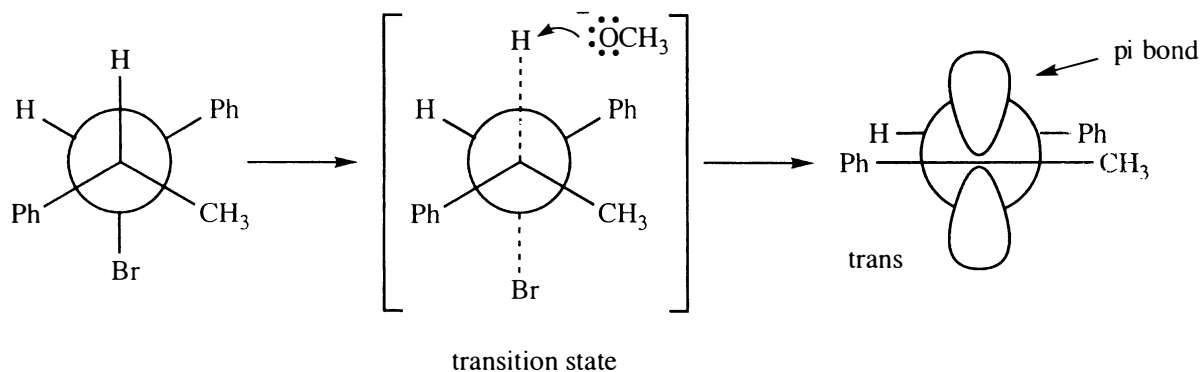
6-37



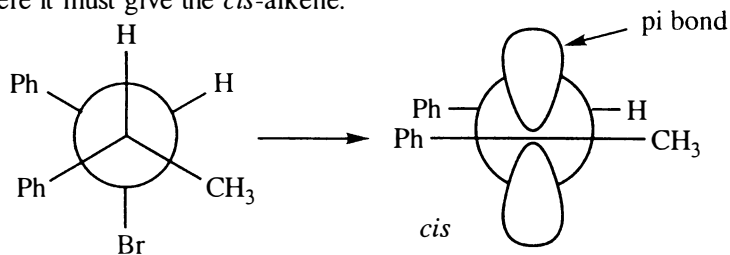
6-38 In systems where free rotation is possible, the H to be abstracted by the base and the leaving group (Br here) must be anti-coplanar. The E2 mechanism is a concerted, one-step mechanism, so the arrangement of the other groups around the carbons in the starting material is retained in the product; there is no intermediate to allow time for rotation of groups. (Models will help.)



orbital picture of this reaction

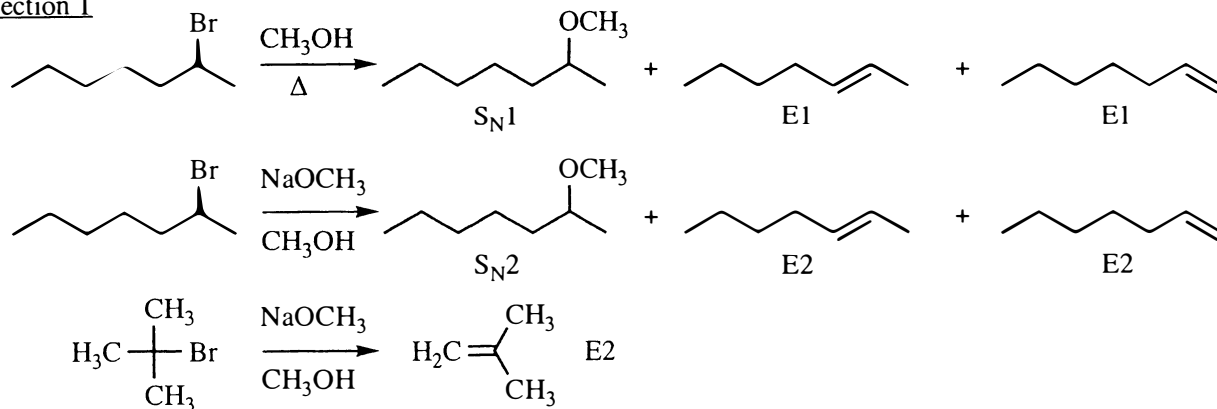


The other diastereomer has two groups interchanged on the back carbon of the Newman projection, where it must give the *cis*-alkene.

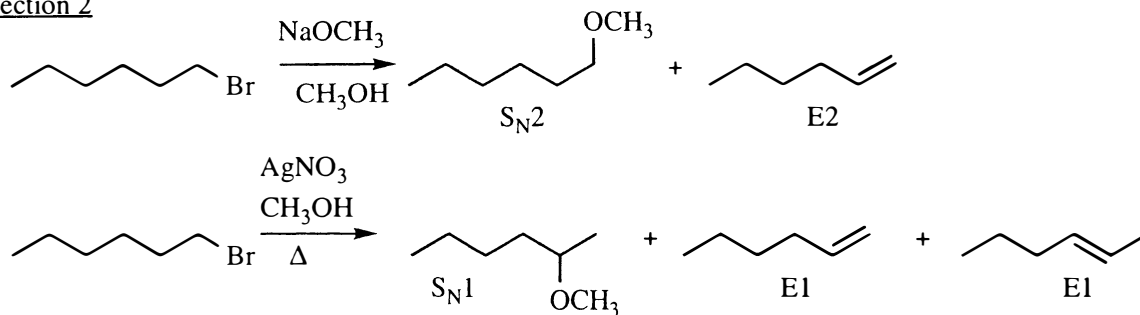


6-39 In this problem, all new internal alkenes form *cis* isomers as well as the *trans* isomers shown.

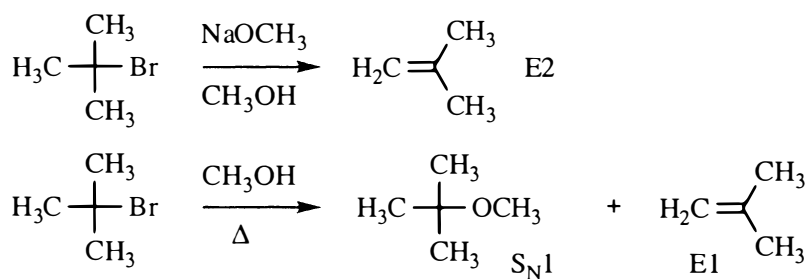
Section 1



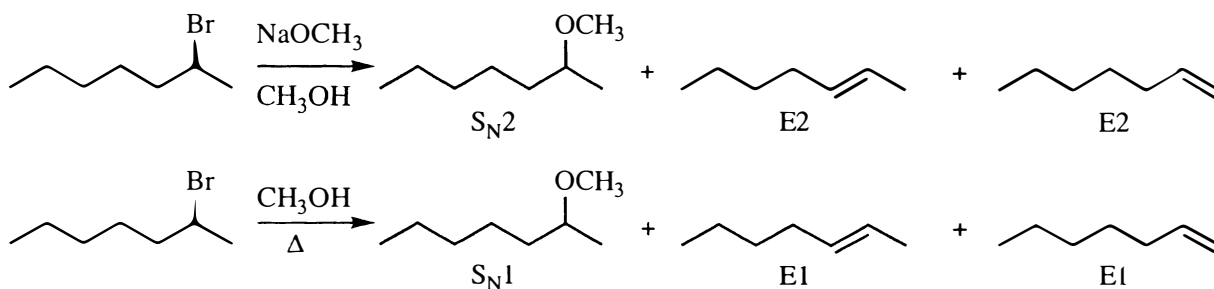
Section 2



Section 3

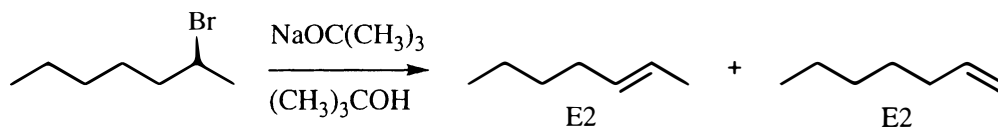
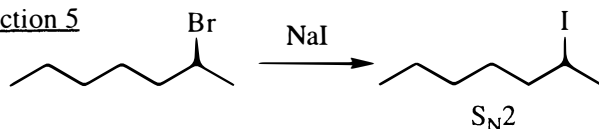


Section 4



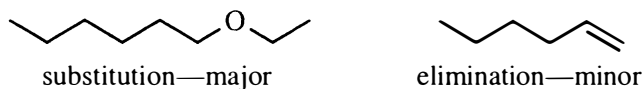
6-39 continued

Section 5

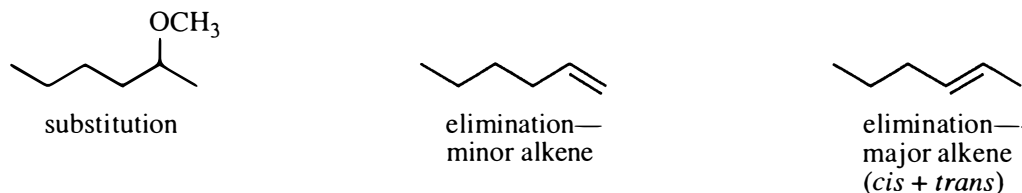


6-40

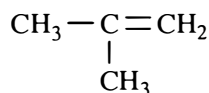
(a) Ethoxide is a strong base/nucleophile—second-order conditions. The 1° bromide favors substitution over elimination, so $\text{S}_{\text{N}}2$ will predominate over $\text{E}2$.



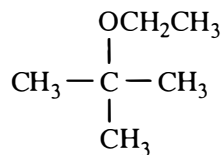
(b) Methoxide is a strong base/nucleophile—second-order conditions. The 2° chloride will undergo $\text{S}_{\text{N}}2$ by backside attack as well as $\text{E}2$ to make a mixture of alkenes.



(c) Ethoxide is a strong base/nucleophile—second-order conditions. The 3° bromide is hindered and cannot undergo $\text{S}_{\text{N}}2$ by backside attack. $\text{E}2$ is the only route possible.



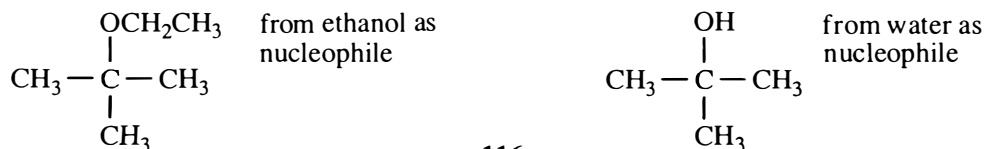
(d) Heating in ethanol is conditions for solvolysis, an $\text{S}_{\text{N}}1$ reaction.



(e) Hydroxide is a strong base/nucleophile—second-order conditions. The 1° iodide is more likely to undergo $\text{S}_{\text{N}}2$ than $\text{E}2$, but both products will be observed.

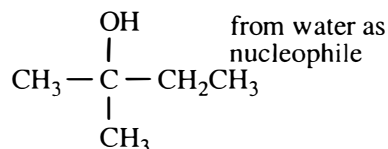
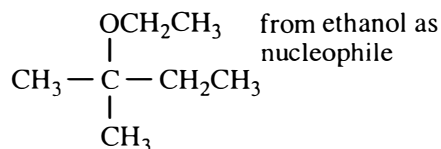


(f) Silver nitrate in ethanol/water is ionizing conditions for 1° alkyl halides that will lead to rearrangement followed by substitution on the 3° carbocation.

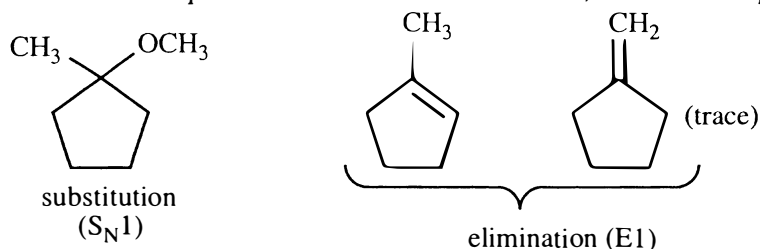


6-40 continued

(g) Silver nitrate in ethanol/water is ionizing conditions for 1° alkyl halides that will lead to rearrangement followed by substitution on the 3° carbocation.



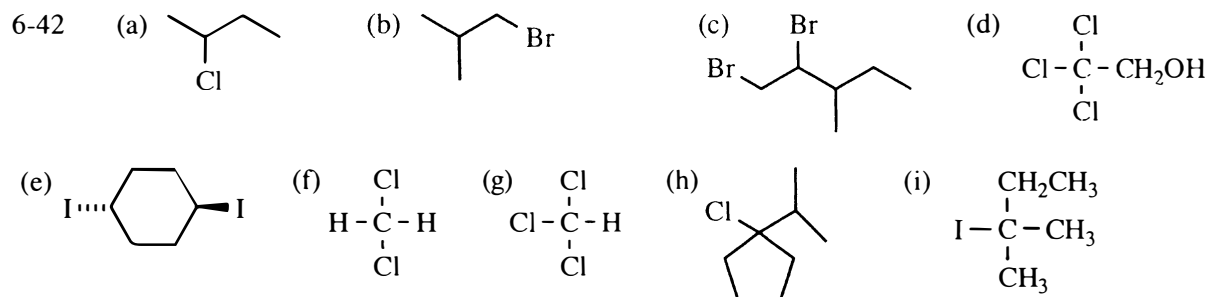
(h) Heating a 3° halide in methanol is quintessential first-order conditions, either E1 or S_N1 (solvolysis).



(i) Ethoxide in ethanol on a 3° halide will lead to E2 elimination; there will be no substitution.



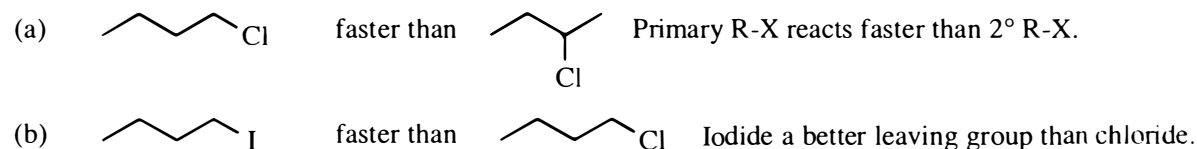
6-41 Please refer to solution 1-20, page 12, of this Solutions Manual.



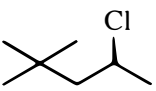
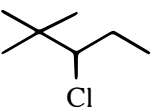
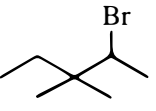
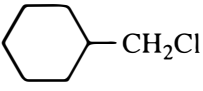
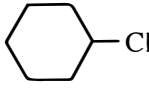
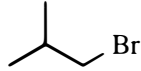
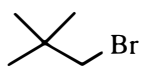
6-43

- | | |
|---------------------------------------|---|
| (a) 2-bromo-2-methylpentane | (d) 4-(2-bromoethyl)-3-(fluoromethyl)-2-methylheptane |
| (b) 1-chloro-1-methylcyclohexane | (e) 4,4-dichloro-5-cyclopropyl-1-iodoheptane |
| (c) 1,1-dichloro-3-fluorocycloheptane | (f) <i>cis</i> -1,2-dichloro-1-methylcyclohexane |

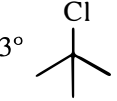
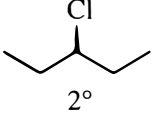
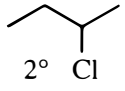
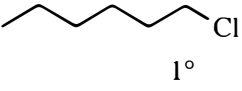
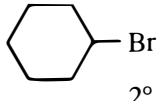
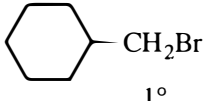
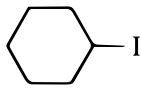
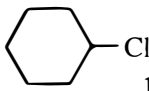
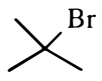
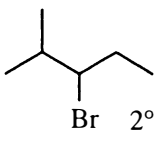
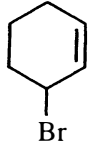
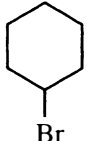
6-44 Ease of backside attack (less steric hindrance) decides which undergoes S_N2 faster in all these examples except (b).



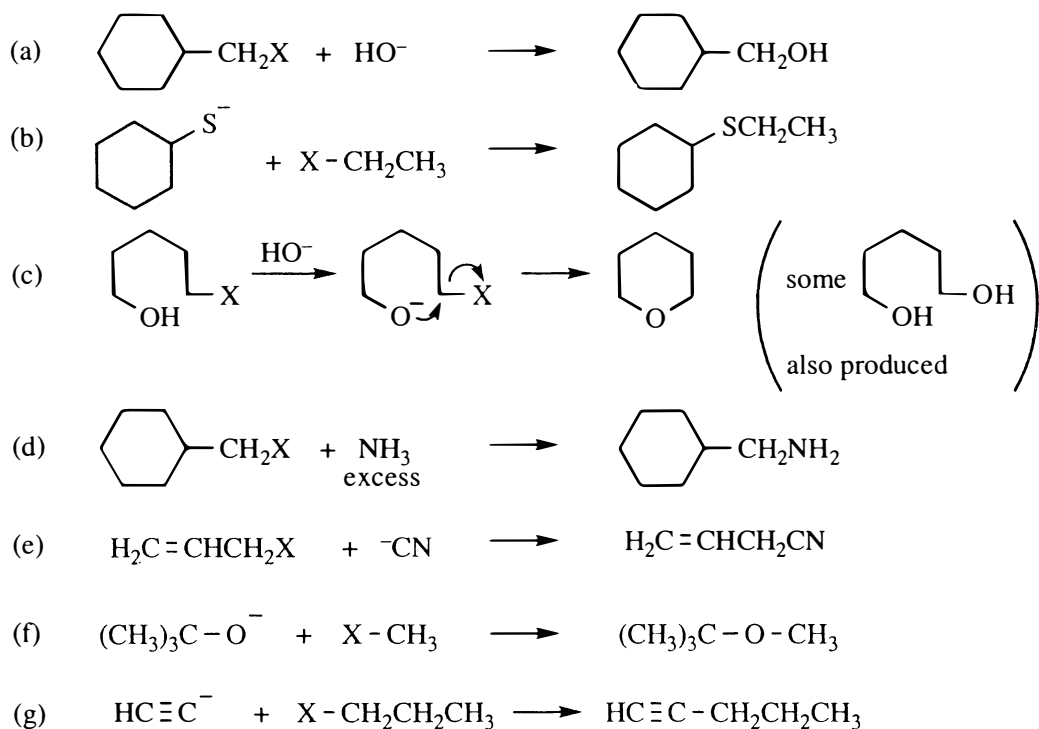
6-44 continued

- (c)  faster than  Less branching on a neighboring carbon.
- (d)  faster than  Same neighboring branching, so 1° faster than 2°.
- (e)  faster than  Primary R-X reacts faster than 2° R-X.
- (f)  faster than  Less branching on a neighboring carbon.

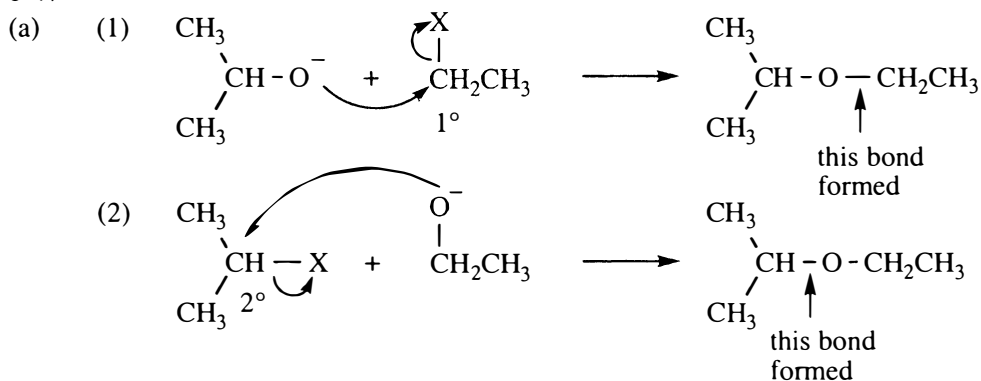
6-45 Formation of the more stable carbocation decides which undergoes S_N1 faster in all these examples except (d).

- (a)  3° faster than  2°
- (b)  2° faster than  1°
- (c)  2° faster than  1°
- (d)  faster than  (leaving group ability)
113
- (e)  3° faster than  2°
- (f)  2° allylic faster than  2°

6-46 For S_N2 , reactions should be designed such that the nucleophile attacks the least highly substituted alkyl halide. ("X" stands for a halide: Cl, Br, or I.)

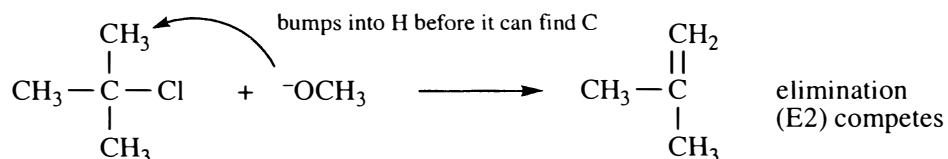


6-47



Synthesis (1) would give a better yield of the desired ether product. (1) uses S_N2 attack of a nucleophile on a 1° carbon, while (2) requires attack on a more hindered 2° carbon. Reaction (2) would give a lower yield of substitution, with more elimination.

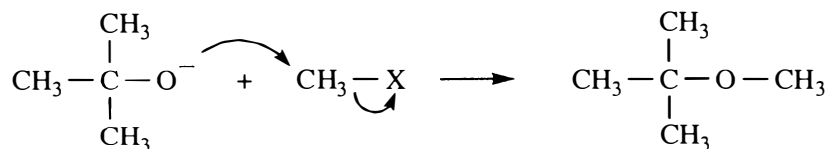
(b) CANNOT DO S_N2 ON A 3° CARBON!



6-47 (b) continued on next page

6-47 (b) continued

Better to do S_N2 on a methyl carbon:



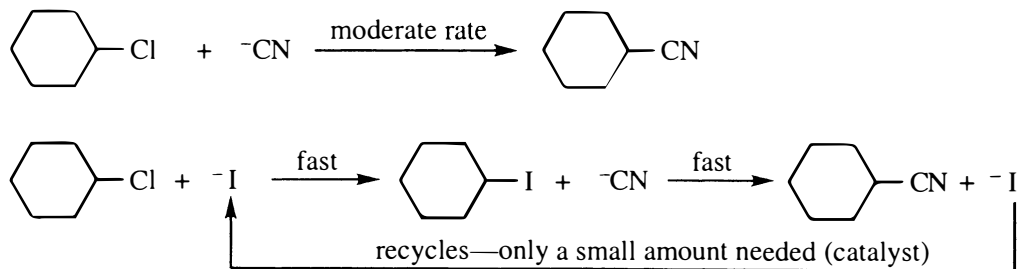
6-48

- (a) S_N2 —second order: reaction rate doubles
- (b) S_N2 —second order: reaction rate increases six times
- (c) Virtually all reaction rates, including this one, increase with a temperature increase.

6-49 This is an S_N1 reaction; the rate law depends only on the substrate concentration, not on the nucleophile concentration.

- (a) no change in rate
- (b) the rate triples, dependent only on [*t*-butyl bromide]
- (c) Virtually all reaction rates, including this one, increase with a temperature increase.

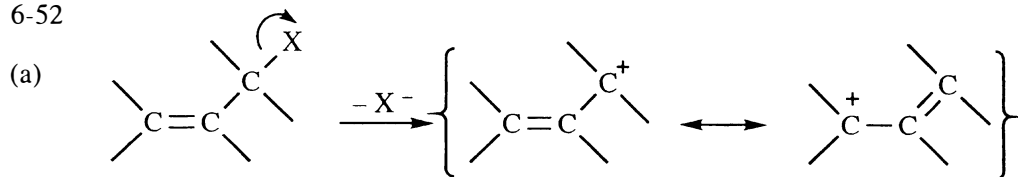
6-50 The key to this problem is that iodide ion is both an excellent nucleophile AND leaving group. Substitution on chlorocyclohexane is faster with iodide than with cyanide (see Table 6-3 for relative nucleophilicities). Once iodocyclohexane is formed, substitution by cyanide is much faster on iodocyclohexane than on chlorocyclohexane because iodide is a better leaving group than chloride. So two fast reactions involving iodide replace a slower single reaction, resulting in an overall rate increase.



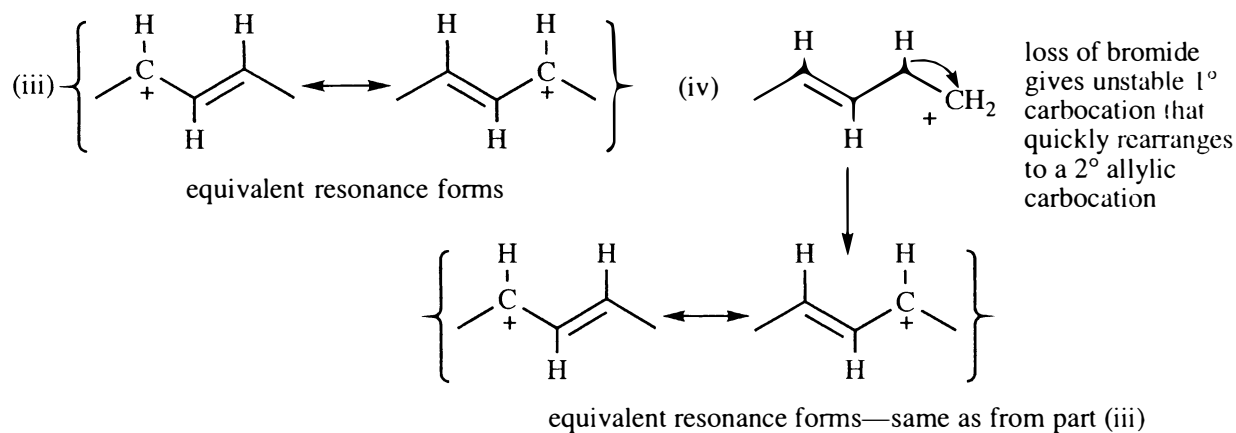
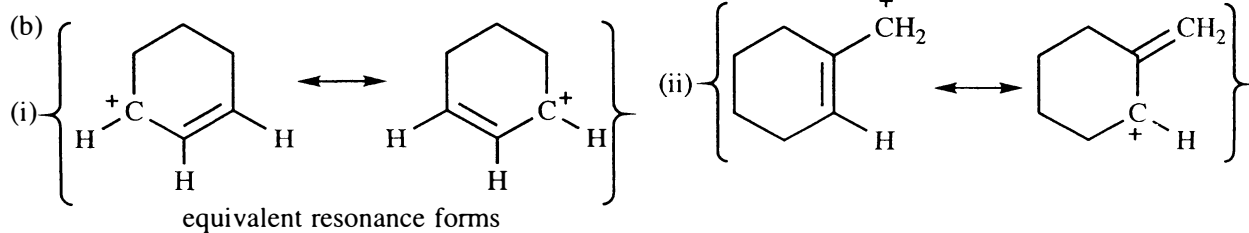
6-51

- (a)
- (b)
- (c) rearrangement
- (d) rearrangement

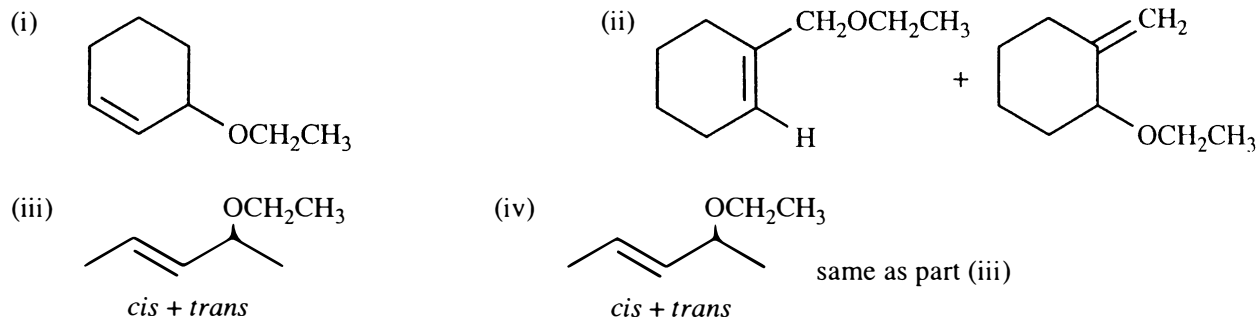
6-52



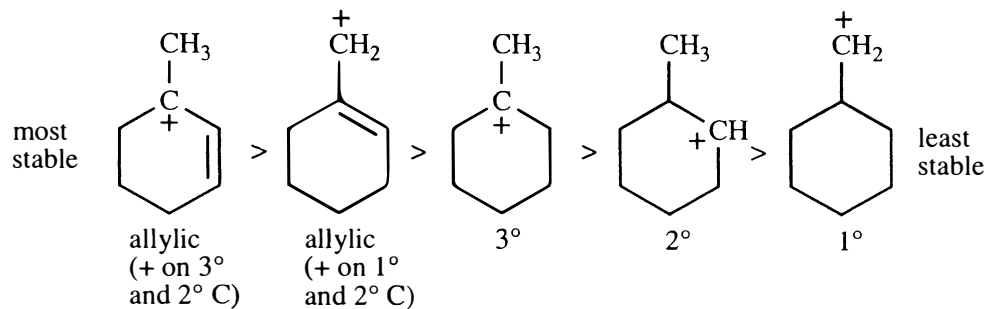
6-52 continued



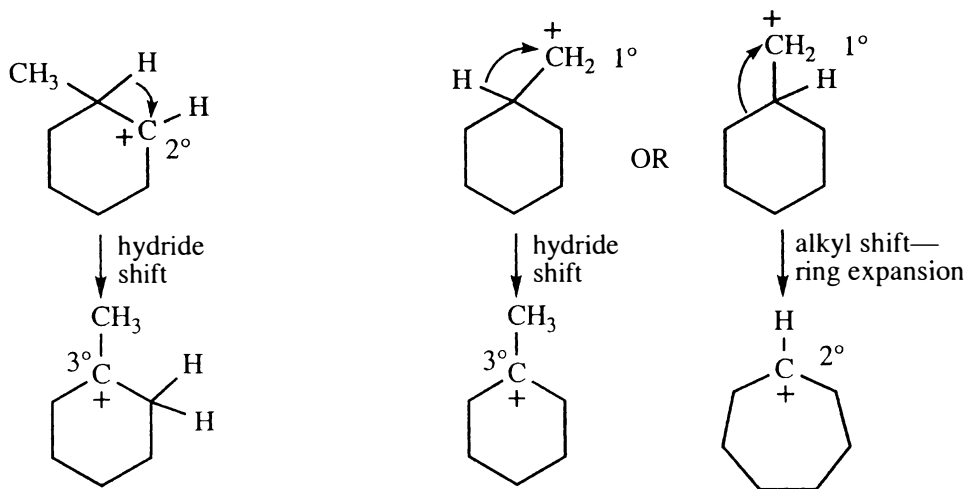
(c) Only one substitution product arises from equivalent resonance forms.



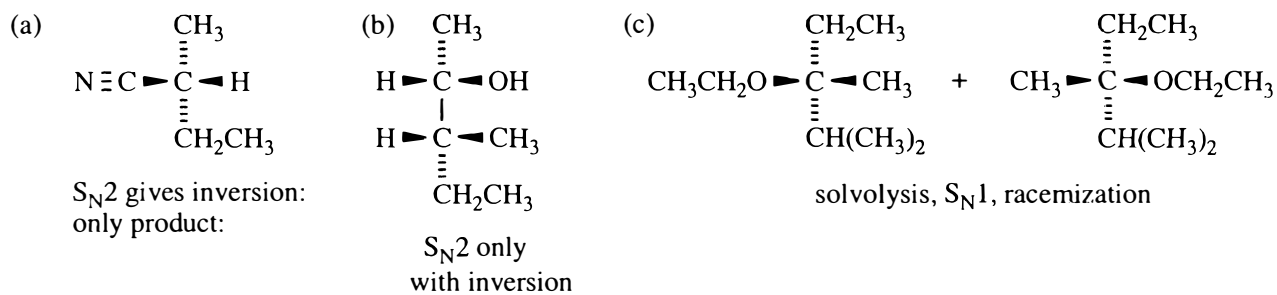
6-53



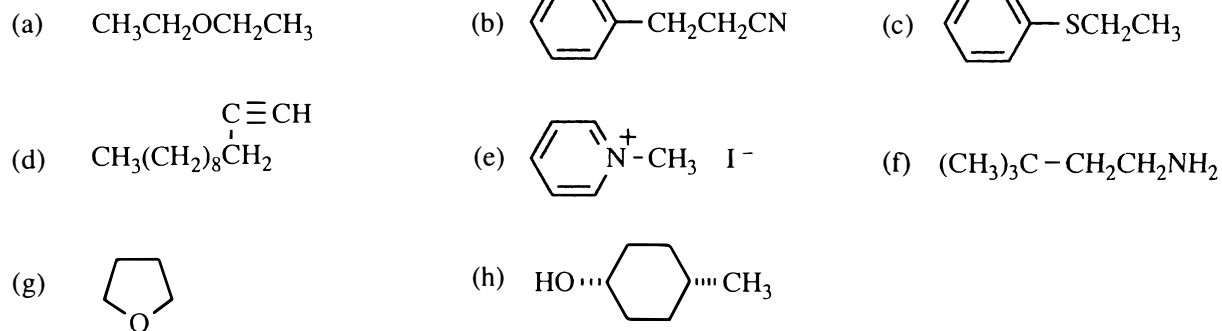
6-54



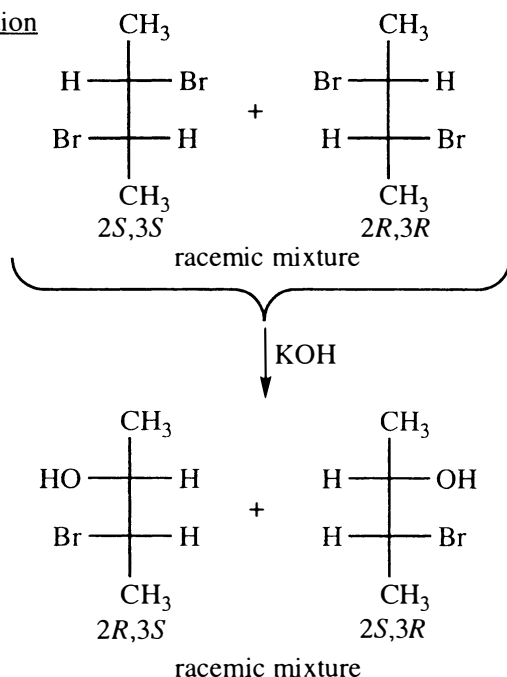
6-55 Reactions would also give some elimination products; only the substitution products are shown here.



6-56

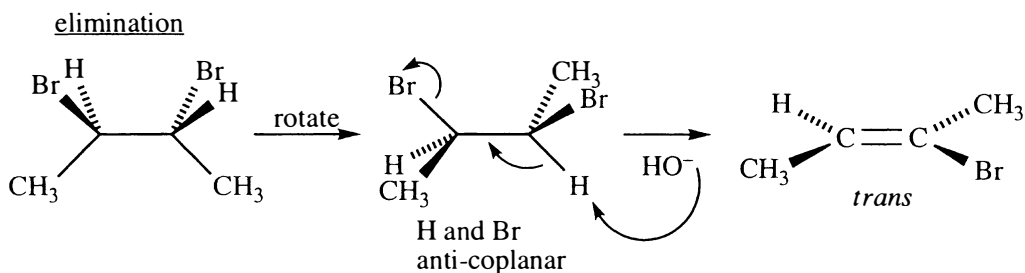


6-57 substitution



Regardless of which bromine is substituted on each molecule, the same mixture of products results.

Each of the substitution products has one chiral center inverted from the starting material. The mechanism that accounts for inversion is S_N2 . If an S_N1 process were occurring, the product mixture would also contain $2R,3R$ and $2S,3S$ diastereomers. Their absence argues against an S_N1 process occurring here.



The other enantiomer gives the same product (you should prove this to yourself).

The absence of *cis* product is evidence that only the E2 elimination is occurring in one step through an anti-coplanar transition state with no chance of rotation. If E1 had been occurring, rotation around the carbocation intermediate would have been possible, leading to both the *cis* and *trans* products.

6-58

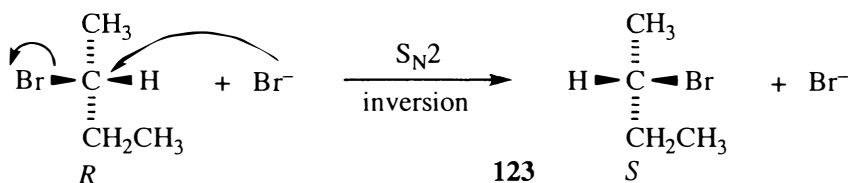
(a)
$$\frac{+15.58^\circ}{+15.90^\circ} \times 100\% = 98\% \text{ of original optical activity} = 98\% \text{ e.e.}$$

Thus, 98% of the *S* enantiomer and 2% racemic mixture gives an overall composition of 99% *S* and 1% *R*.

(b) The 1% of radioactive iodide has produced exactly 1% of the *R* enantiomer. Each substitution must occur with inversion, a classic S_N2 mechanism.

6-59

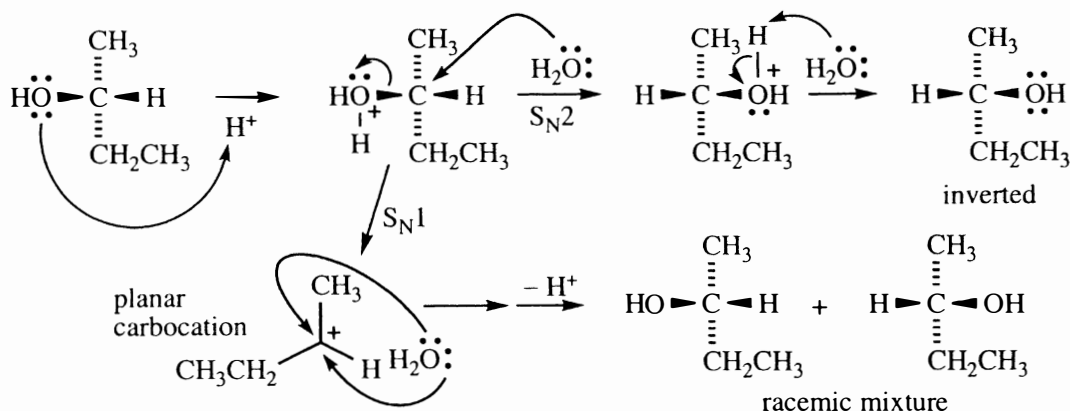
(a) An S_N2 mechanism with inversion will convert *R* to its enantiomer, *S*. An accumulation of excess *S* does not occur because it can also react with bromide, regenerating *R*. The system approaches a racemic mixture at equilibrium.



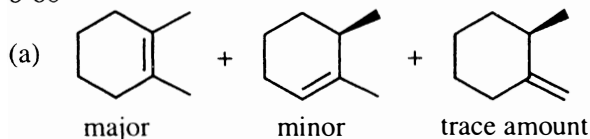
6-59 continued

(b) In order to undergo substitution and therefore inversion, HO^- would have to be the leaving group, but HO^- is never a leaving group in $\text{S}_{\text{N}}2$. No reaction can occur.

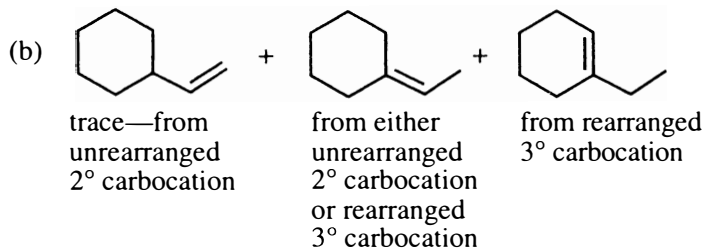
(c) Once the OH is protonated, it can leave as H_2O . Racemization occurs in the $\text{S}_{\text{N}}1$ mechanism because of the planar, achiral carbocation intermediate which "erases" all stereochemistry of the starting material. Racemization occurs in the $\text{S}_{\text{N}}2$ mechanism by establishing an equilibrium of *R* and *S* enantiomers, as explained in 6-59(a).



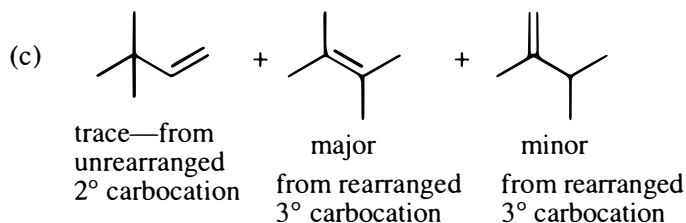
6-60



The carbocation produced in this E1 elimination is 3° and will not rearrange. The product ratio follows the Zaitsev rule.

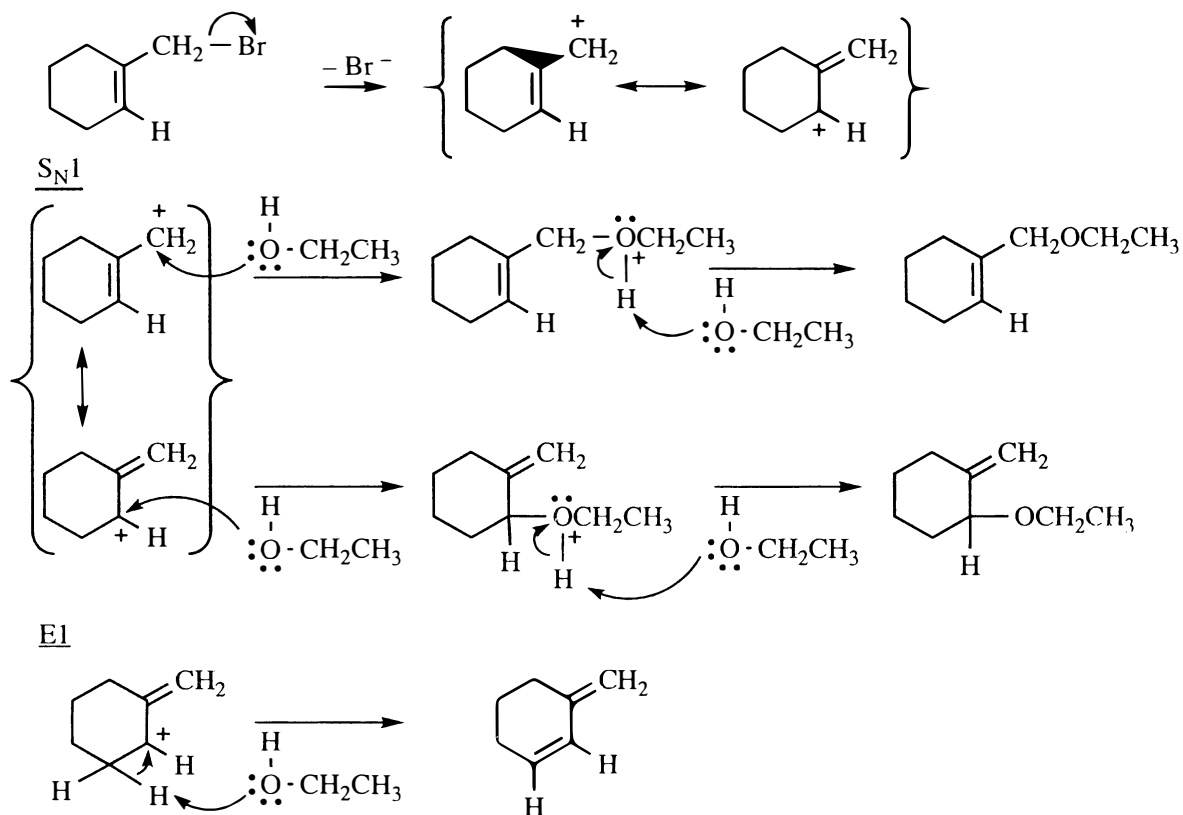


The carbocation produced in this E1 elimination is 2° and can either eliminate to give the first two alkenes, or can rearrange by a hydride shift to a 3° carbocation which would produce the last two products. The amounts of the last two products are not predictable as they are both trisubstituted, but the first product will certainly be the least.

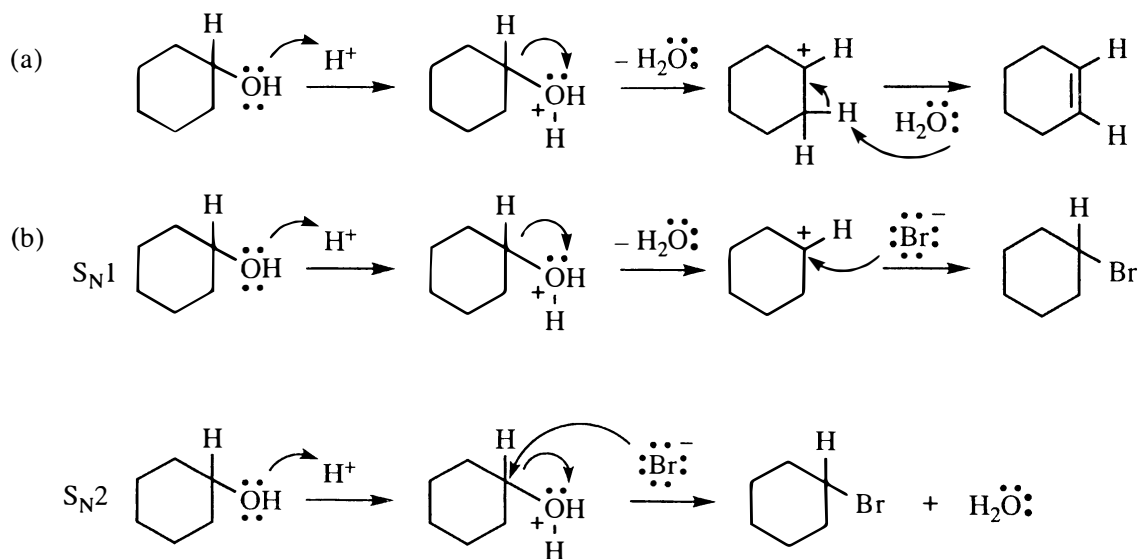


The carbocation produced in this E1 elimination is 2° and can either eliminate to give the first alkene, or can rearrange by a methyl shift to a 3° carbocation which would produce the last two products. The middle product is major as it is tetrasubstituted versus disubstituted for the last structure and monosubstituted for the first structure.

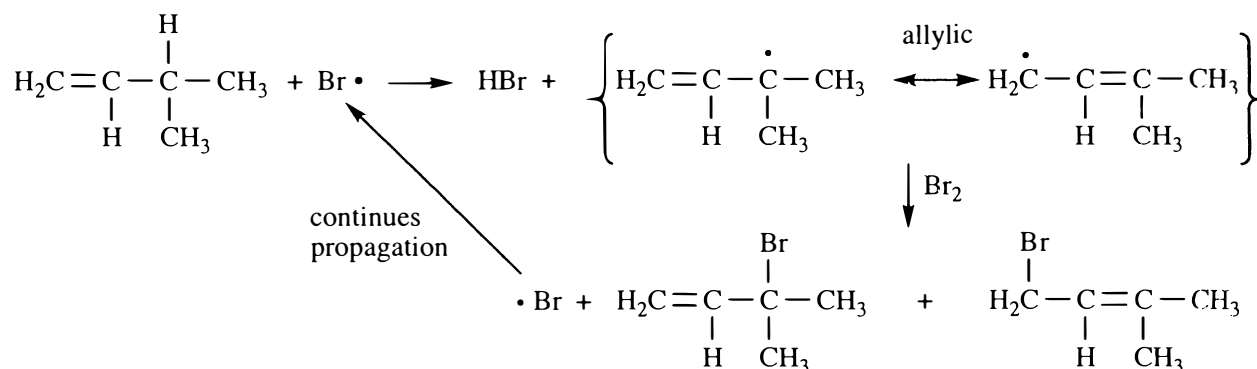
6-61 The allylic carbocation has two resonance forms showing that two carbons share the positive charge. The ethanol nucleophile can attack either of these carbons, giving the S_N1 products; or loss of an adjacent H will give the E1 product.



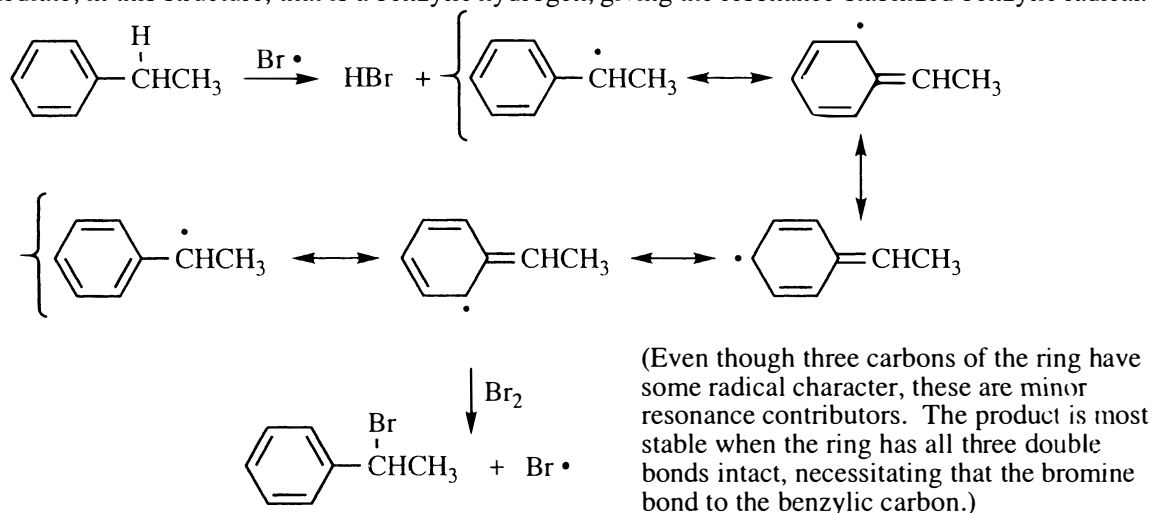
6-62



6-63 NBS generates bromine which produces bromine radical. Bromine radical abstracts an allylic hydrogen, resulting in a resonance-stabilized allylic radical. The allylic radical can bond to bromine at either of the two carbons with radical character.

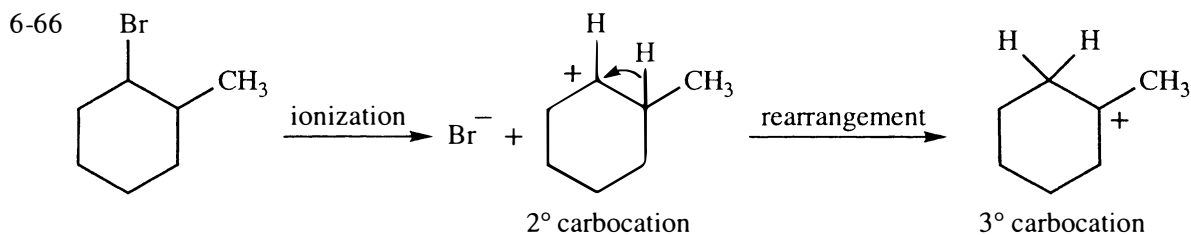


6-64 The bromine radical from NBS will abstract whichever hydrogen produces the most stable intermediate; in this structure, that is a benzylic hydrogen, giving the resonance-stabilized benzylic radical.



6-65 Two related factors could explain this observation. First, as carbocation stability increases, the leaving group will be less tightly held by the carbocation for stabilization; the more stable carbocations are more "free" in solution, meaning more exposed. Second, more stable carbocations will have longer lifetimes, allowing the leaving group to drift off in the solvent, leading to more possibility for the incoming nucleophile to attack from the side that the leaving group just left.

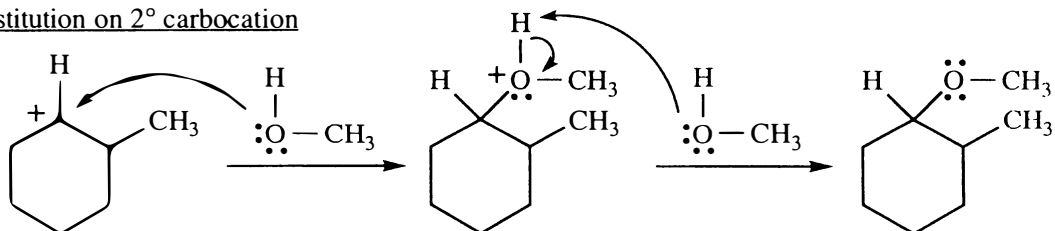
The less stable carbocations hold tightly to their leaving groups, preventing nucleophiles from attacking this side. Backside attack with inversion is the preferred stereochemical route in this case.



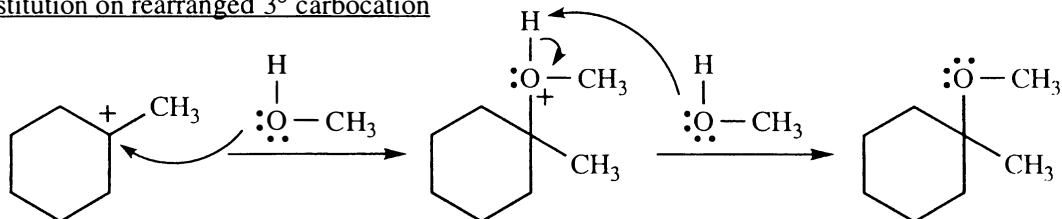
mechanisms continued
on next page

6-66 continued

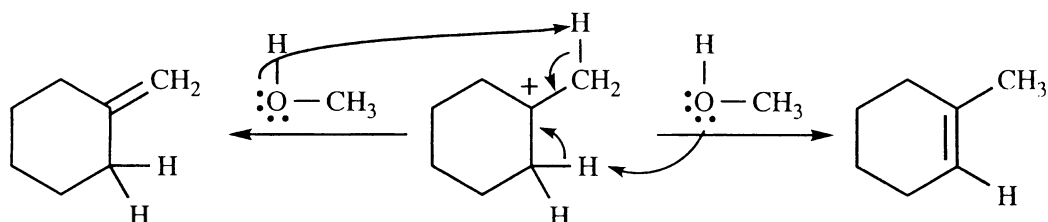
substitution on 2° carbocation



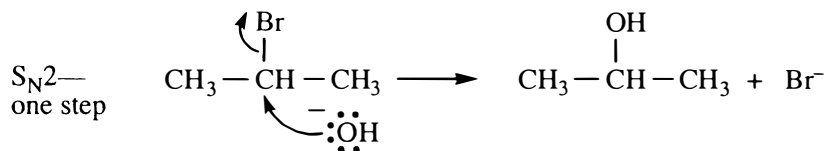
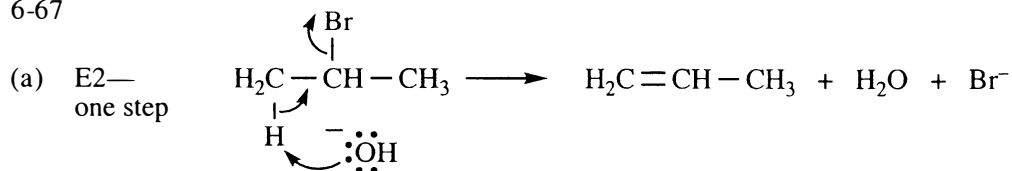
substitution on rearranged 3° carbocation



elimination from rearranged 3° carbocation

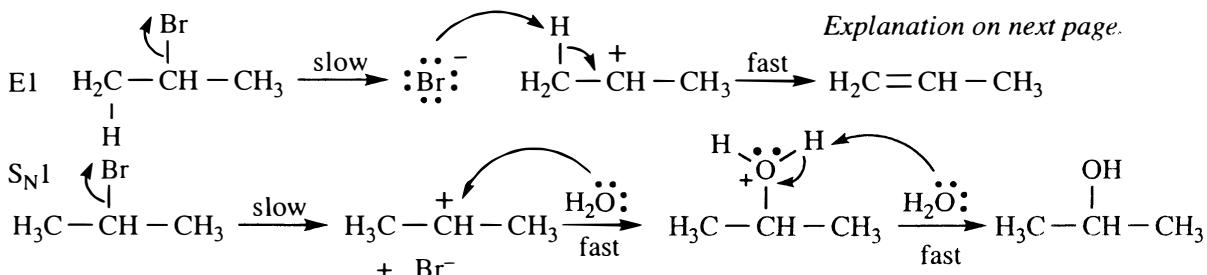


6-67



(b) In the E2 reaction, a C—H bond is broken. When D is substituted for H, a C—D bond is broken, slowing the reaction. In the S_N2 reaction, no C—H (C—D) bond is broken, so the rate is unchanged.

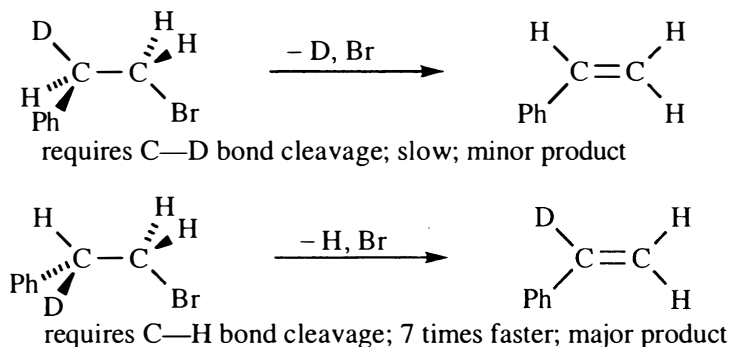
(c) These are first-order reactions. The slow, rate-determining step is the first step in each mechanism.



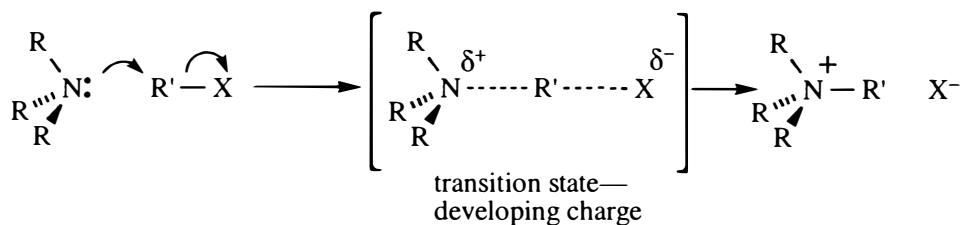
6-67 (c) continued

The only mechanism of these two involving C—H bond cleavage is the E1, but the C—H cleavage does NOT occur in the slow, rate-determining step. Kinetic isotope effects are observed only when C—H (C—D) bond cleavage occurs in the rate-determining step. Thus, we would expect to observe *no change in rate* for the deuterium-substituted molecules in the E1 or S_N1 mechanisms. (In fact, this technique of measuring isotope effects is one of the most useful tools chemists have for determining what mechanism a reaction follows.)

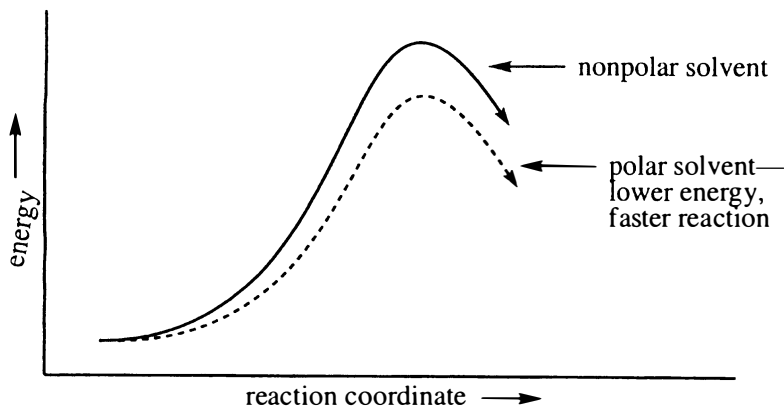
6-68 Both products are formed through E2 reactions. The difference is whether a D or an H is removed by the base. As explained in Problem 6-67, C—D cleavage can be up to 7 times slower than C—H cleavage, so the product from C—H cleavage should be formed about 7 times as fast. This rate preference is reflected in the 7 : 1 product mixture. ("Ph" is the abbreviation for a benzene ring.)



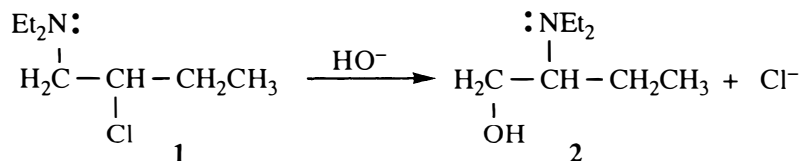
6-69 The energy, and therefore the structure, of the transition state determines the rate of a reaction. Any factor which lowers the energy of the transition state will speed the reaction.



This example of S_N2 is unusual in that the nucleophile is a neutral molecule—it is not negatively charged. The transition state is beginning to show the positive and negative charges of the products (ions), so the transition state is more charged than the reactants. The polar transition state will be stabilized in a more polar solvent through dipole-dipole interactions, so the rate of reaction will be enhanced in a polar solvent.



6-70 The problem is how to explain this reaction:

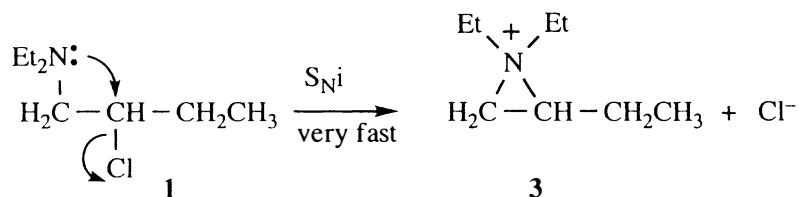


facts

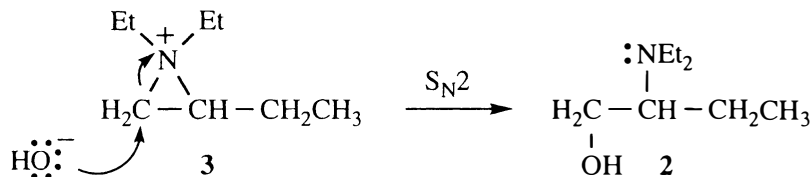
- 1) second order, but several thousand times faster than similar second order reactions without the NEt₂ group
- 2) NEt₂ group migrates

Solution

Clearly, the NEt₂ group is involved. The nitrogen is a nucleophile and can do an internal nucleophilic substitution (S_Ni), a very fast reaction for entropy reasons because two different molecules do not have to come together.



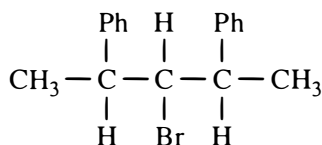
The slower step is attack of HO⁻ on intermediate **3**; the N is a good leaving group because it has a positive charge. Where will HO⁻ attack **3**? On the less substituted carbon, in typical S_N2 fashion.



This overall reaction is fast because of the *neighboring group assistance* in forming **3**. It is second order because the HO⁻ group and **3** collide in the slow step (not the *only* step, however). And the NEt₂ group "migrates", although in two steps.

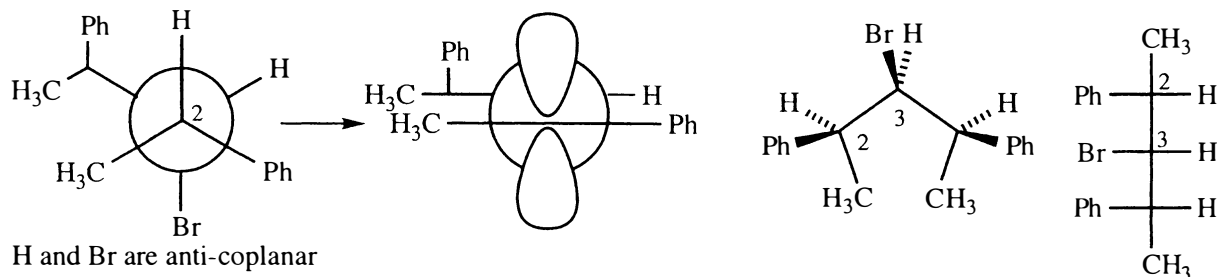
6-71 The symmetry of this molecule is crucial.

(a)

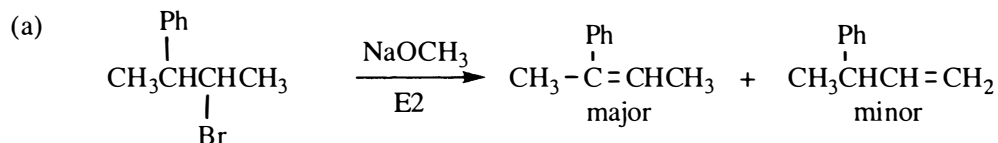


Regardless of which adjacent H is removed by *t*-butoxide, the product will be 2,4-diphenyl-2-pentene.

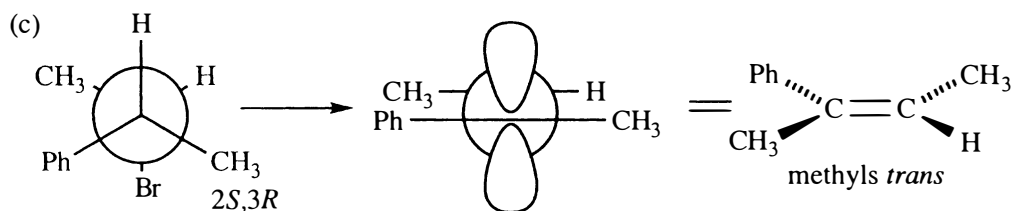
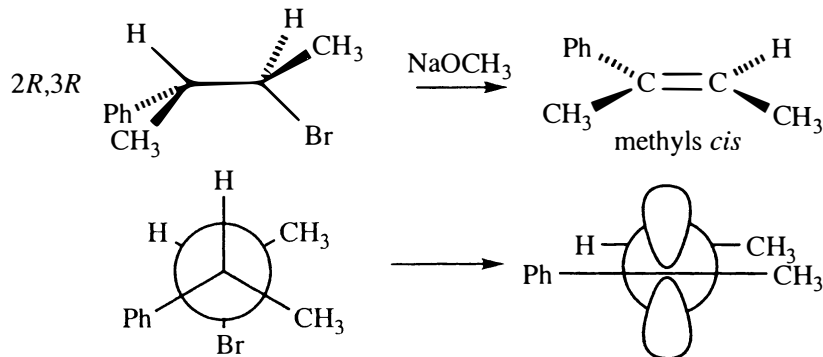
(b) Here are a Newman projection, a three-dimensional representation and a Fischer projection of the required diastereomer. On both carbons 2 and 4, the H has to be anti-coplanar with the bromine while leaving the other groups to give the same product. Not coincidentally, the correct diastereomer is a meso structure.



6-72 "Ph" = phenyl

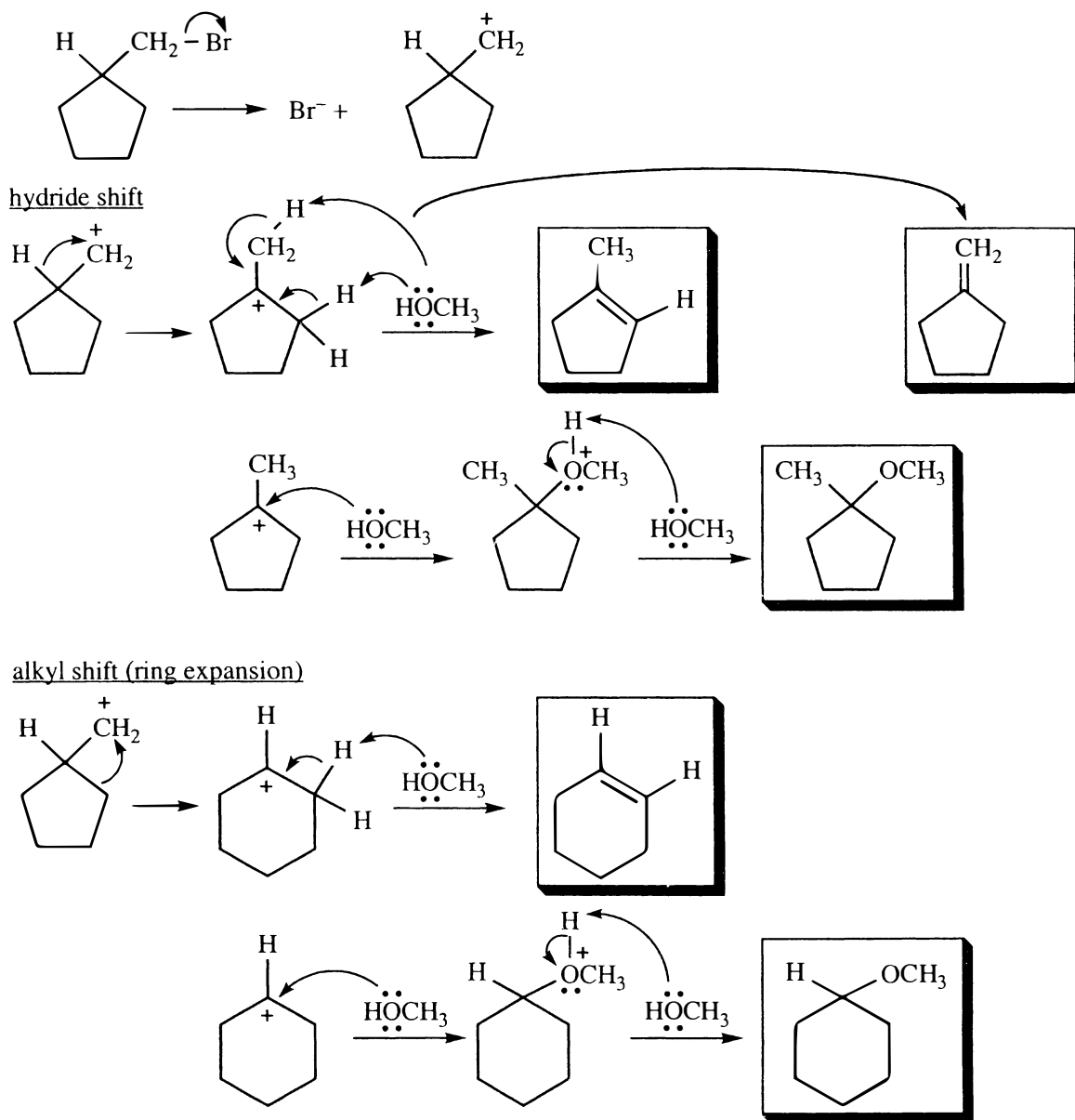


(b) H and Br must be anti-coplanar in the transition state

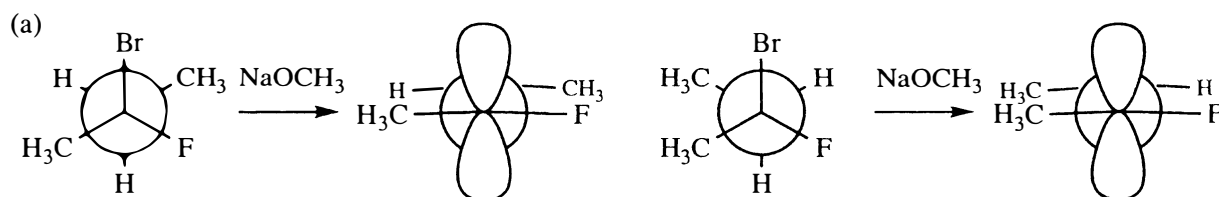


(d) The 2*S*,3*S* is the mirror image of 2*R*,3*R*; it would give the mirror image of the alkene that 2*R*,3*R* produced (with two methyl groups *cis*). The alkene product is planar, not chiral, so its mirror image is the same: the 2*S*,3*S* and the 2*R*,3*R* give the same alkene.

6-73 All five products (boxed) come from rearranged carbocations. Rearrangement, which may occur simultaneously with ionization, can occur by hydride shift to the 3° methylcyclopentyl cation, or by ring expansion to the cyclohexyl cation.

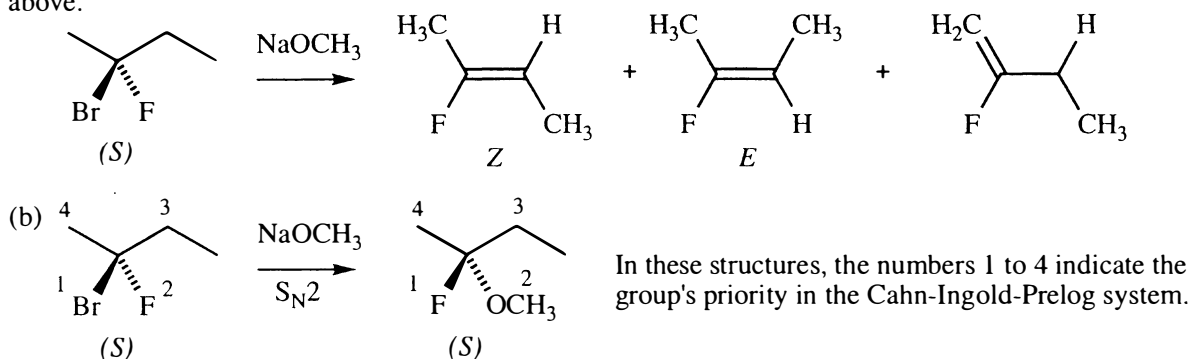


6-74 Begin with a structure of (*S*)-2-bromo-2-fluorobutane. Since there is no H on C-2, the lowest priority group must be the CH_3 . The Br has highest priority, then F, then CH_2CH_3 , and CH_3 is fourth. Sodium methoxide is a strong base and nucleophile, so the reaction must be second order, E_2 or $\text{S}_{\text{N}}2$.



6-74 continued

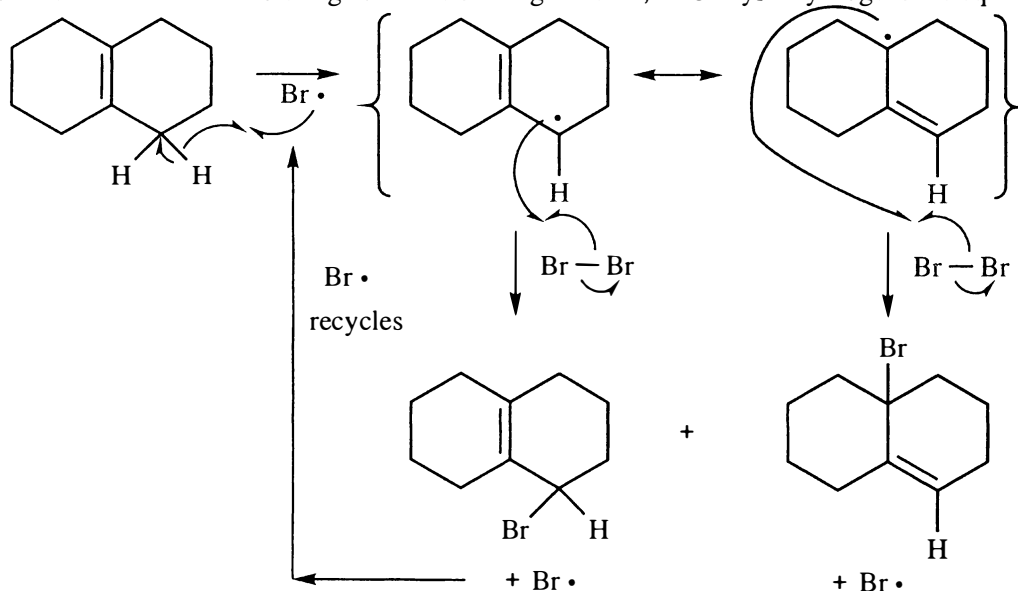
In regular structural formulas, the reaction would give three products including the stereoisomers shown above.



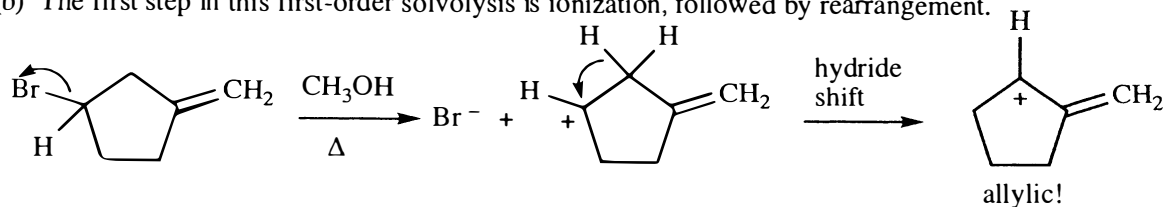
A cursory analysis of the *designation* of configuration would suggest to the uncritical mind that this reaction proceeded with retention of configuration—but that would be wrong! You know by now that a careful analysis is required. In the Cahn-Ingold-Prelog system, the F in the starting material was priority group 2, but in the product, because Br has left, F is now the first priority group. So even though the *designation* of configuration suggests retention of configuration, the molecule has actually undergone inversion as would be expected with an S_N2 reaction. (See the solution to problem 6-21 for a similar example.)

6-75

(a) Only the propagation steps are shown. NBS provides a low concentration of Br_2 which generates bromine radical in ultraviolet light. In the starting material, all 8 allylic hydrogens are equivalent.



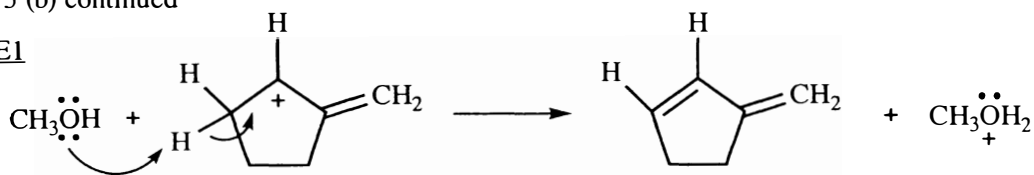
(b) The first step in this first-order solvolysis is ionization, followed by rearrangement.



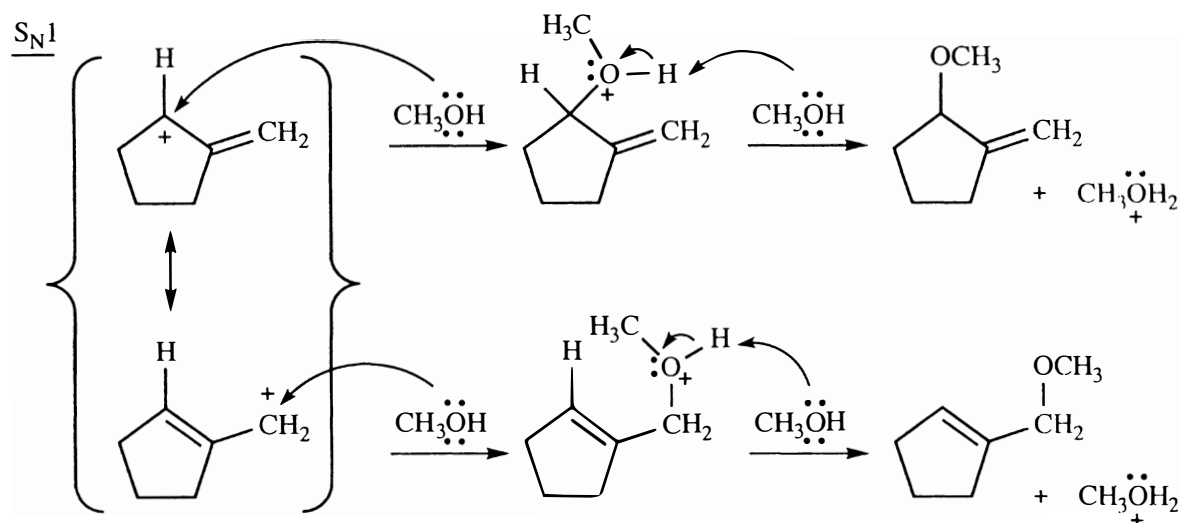
mechanism continued on next page

6-75 (b) continued

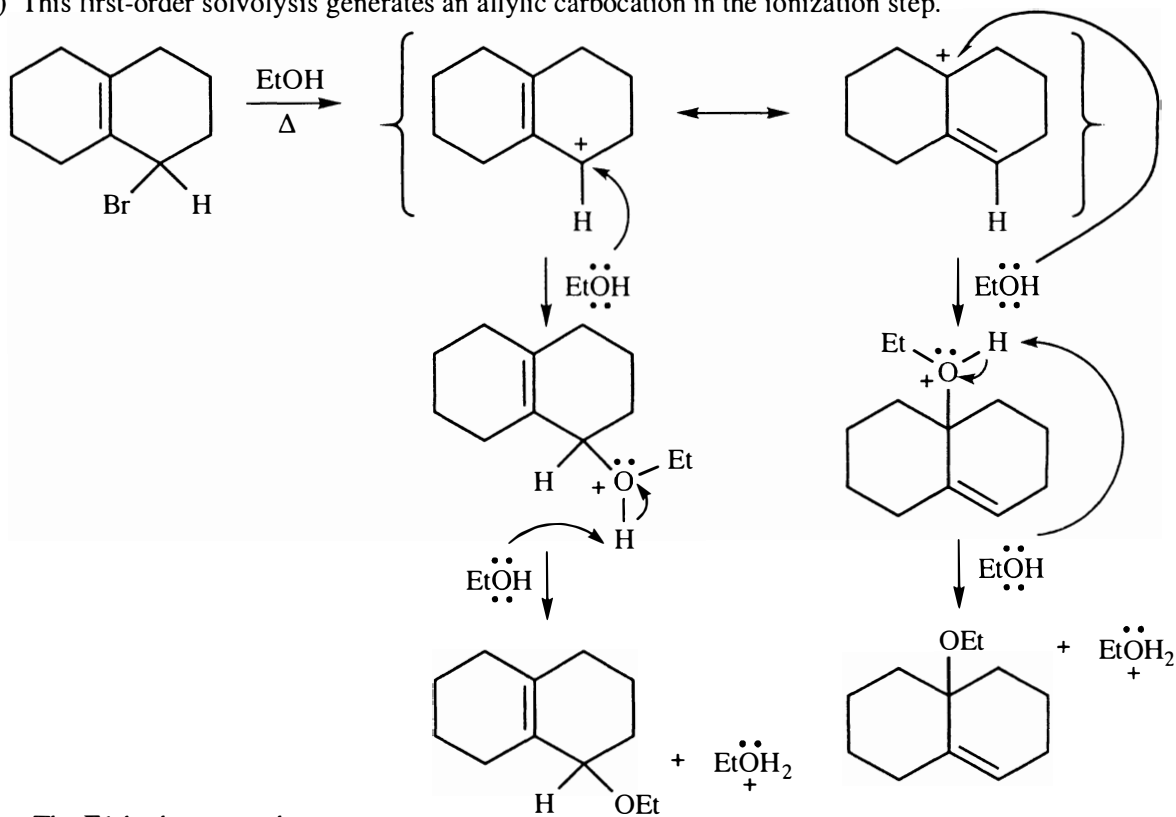
E1



S_N1



(c) This first-order solvolysis generates an allylic carbocation in the ionization step.

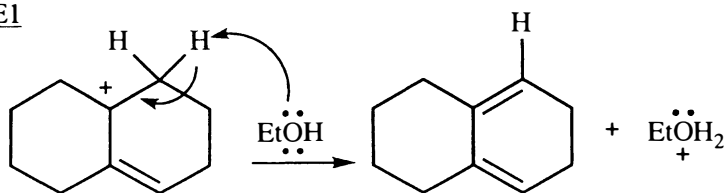


The E1 is shown on the next page.

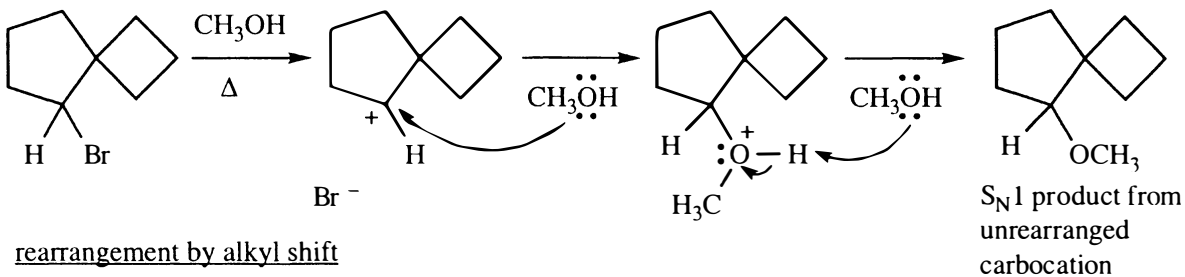
These are the S_N1 products.

6-75 (c) continued

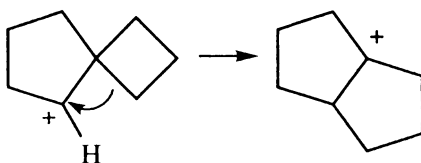
E1



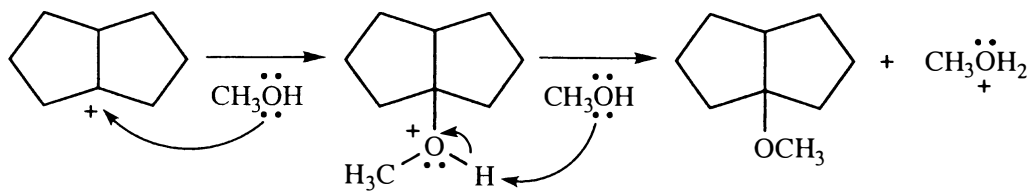
(d) The first step in this first-order solvolysis is ionization, followed by rearrangement.



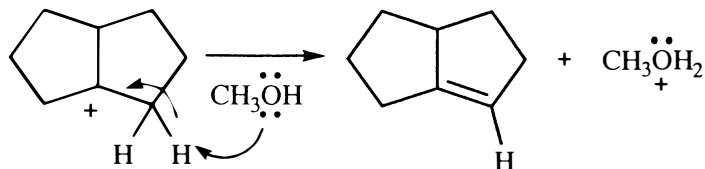
rearrangement by alkyl shift



S_N1 on rearranged carbocation



E1 on rearranged carbocation



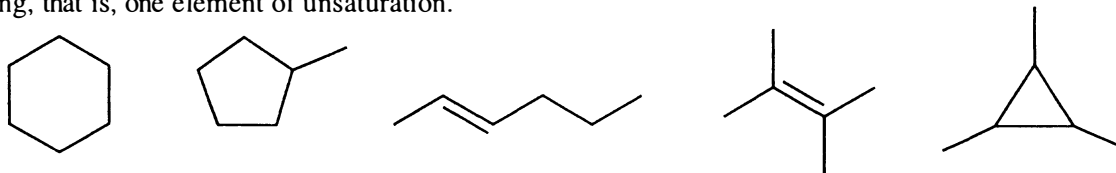
CHAPTER 7—STRUCTURE AND SYNTHESIS OF ALKENES

7-1 The number of elements of unsaturation in a hydrocarbon formula is given by:

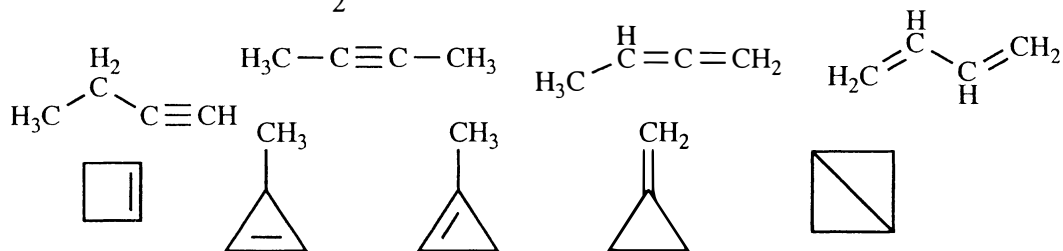
$$\frac{2(\#C) + 2 - (\#H)}{2}$$

(a) $C_6H_{12} \Rightarrow \frac{2(6) + 2 - (12)}{2} = 1 \text{ element of unsaturation}$

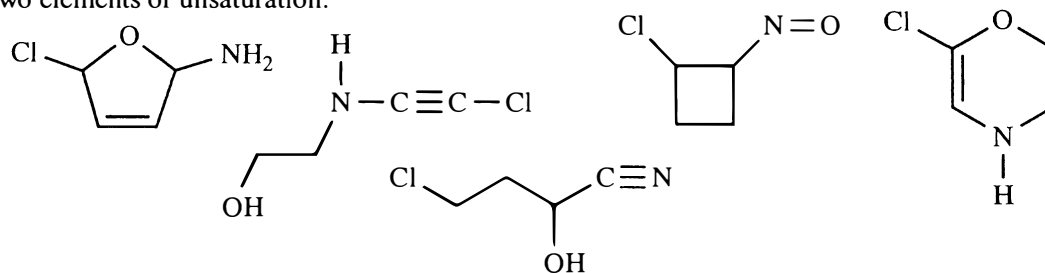
(b) Many examples are possible. Yours may not match these, but all must have either a double bond or a ring, that is, one element of unsaturation.



7-2 $C_4H_6 \Rightarrow \frac{2(4) + 2 - (6)}{2} = 2 \text{ elements of unsaturation}$

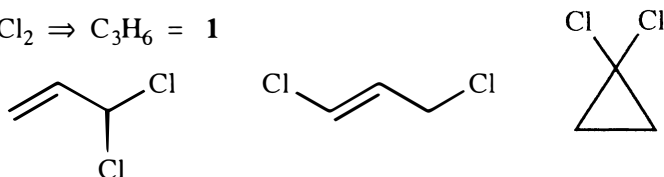


7-3 Hundreds of examples of C_4H_6NOCl are possible. Yours may not match these, but all must contain two elements of unsaturation.

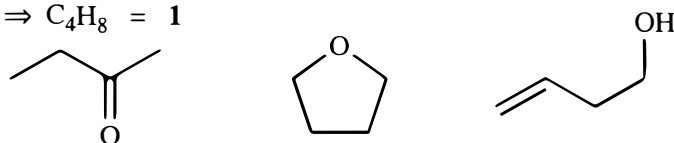


7-4 Many examples of these formulas are possible. Yours may not match these, but correct answers must have the same number of elements of unsaturation.

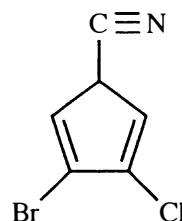
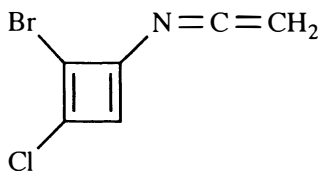
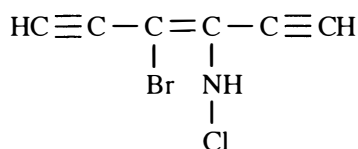
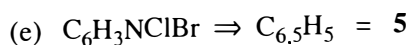
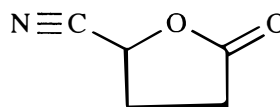
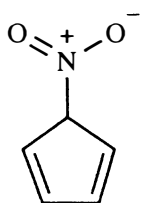
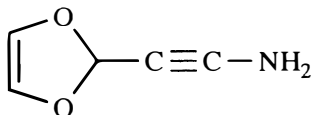
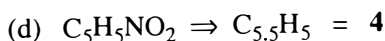
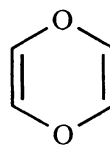
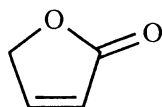
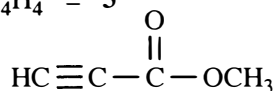
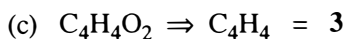
(a) $C_3H_4Cl_2 \Rightarrow C_3H_6 = 1$



(b) $C_4H_8O \Rightarrow C_4H_8 = 1$



7-4 continued

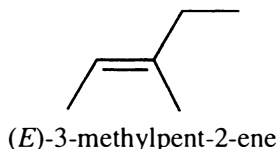
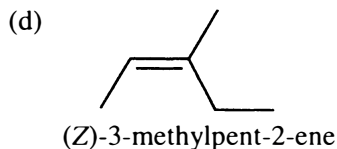
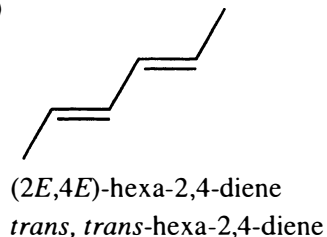
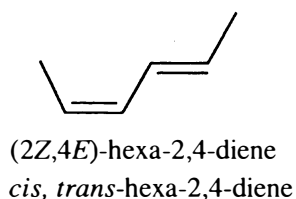
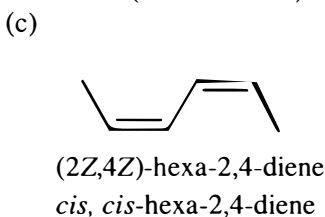
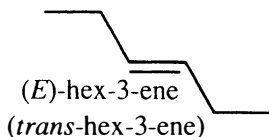
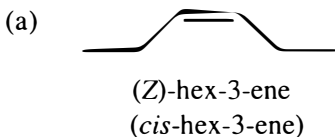


Note to the student: The IUPAC system of nomenclature is undergoing many changes, most notably in the placement of position numbers. The new system places the position number close to the functional group designation, which is what this Solutions Manual will attempt to follow; however, you should be able to use and recognize names in either the old or the new style. Ask your instructor which system to use.

7-5

- | | |
|--------------------------------------|---|
| (a) 4-methylpent-1-ene | (f) 4-vinylcyclohex-1-ene ("1" is optional) |
| (b) 2-ethylhex-1-ene | (g) 3-phenylprop-1-ene ("1" is optional) |
| (c) penta-1,4-diene | (h) <i>trans</i> -3,4-dimethylcyclopent-1-ene ("1" is optional) |
| (d) penta-1,2,4-triene | (i) 7-methylenecyclohepta-1,3,5-triene |
| (e) 2,5-dimethylcyclopenta-1,3-diene | |

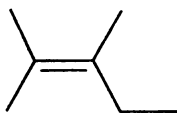
7-6 (b), (e), and (f) do not show *cis,trans* isomerism



"*Cis*" and "*trans*" are not clear for this example;
"*E*" and "*Z*" are unambiguous.

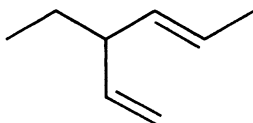
7-7

(a)



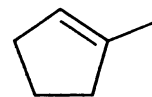
2,3-dimethylpent-2-ene
(neither *cis* nor *trans*)

(b)



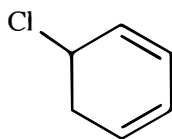
3-ethylhexa-1,4-diene
(*cis* or *trans* not specified; the vinyl group is part of the main chain)

(c)



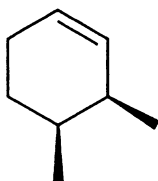
1-methylcyclopentene

(d)



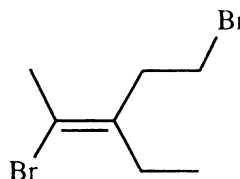
5-chlorocyclohexa-1,3-diene
(positions of double bonds need to be specified)

(e)



cis-3,4-dimethylcyclohexene
(could also have drawn *trans*)

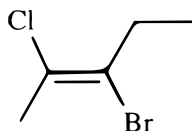
(f)



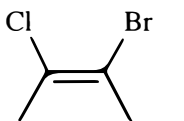
(*E*)-2,5-dibromo-3-ethylpent-2-ene
(*cis* does not apply)

7-8

(a)

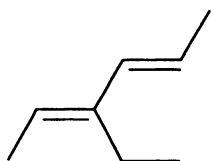


(*E*)-3-bromo-2-chloropent-2-ene

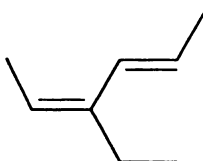


(*Z*)-3-bromo-2-chloropent-2-ene

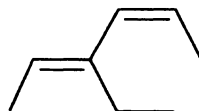
(b)



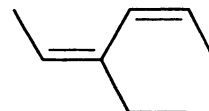
(2*E*,4*E*)-3-ethylhexa-2,4-diene



(2*Z*,4*E*)-



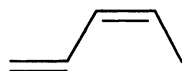
(2*E*,4*Z*)-



(2*Z*,4*Z*)-

(c) no geometric isomers

(d)

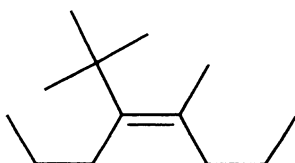


(*Z*)-penta-1,3-diene

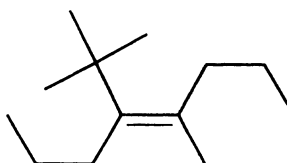


(*E*)-penta-1,3-diene

(e)



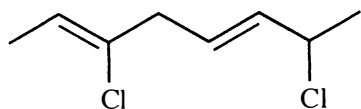
(*E*)-4-*t*-butyl-5-methyloct-4-ene



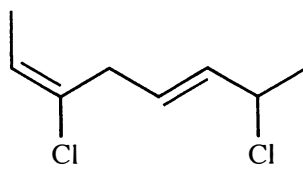
(*Z*)-4-*t*-butyl-5-methyloct-4-ene

7-8 continued

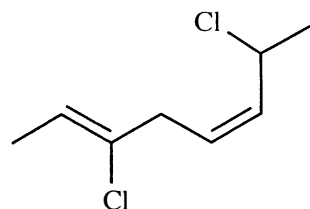
(f)



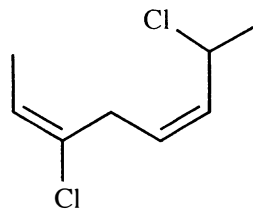
(2Z,5E)-3,7-dichloroocta-2,5-diene



(2E,5E)-3,7-dichloroocta-2,5-diene



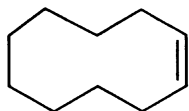
(2Z,5Z)-3,7-dichloroocta-2,5-diene



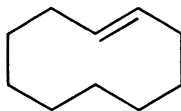
(2E,5Z)-3,7-dichloroocta-2,5-diene

(g) no geometric isomers (an *E* double bond would be too highly strained)

(h)

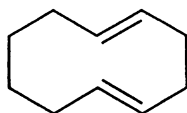


(Z)-cyclodecene

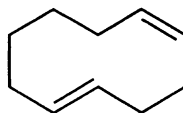


(E)-cyclodecene

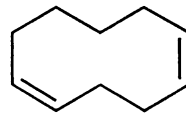
(i)



(1E,5E)-cyclodeca-1,5-diene

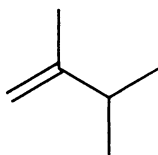


(1Z,5E)-cyclodeca-1,5-diene

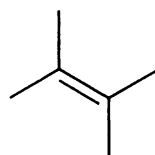


(1Z,5Z)-cyclodeca-1,5-diene

7-9 From Table 7-1, approximate heats of hydrogenation can be determined for similarly substituted alkenes. The energy difference is approximately 6 kJ/mole (1.4 kcal/mole), the more highly substituted alkene being more stable.



gem-disubstituted
117 kJ/mole
(28.0 kcal/mole)



tetrasubstituted
111 kJ/mole
(26.6 kcal/mole)

7-10 Use the relative values in Figure 7-7.

(a) 2 x (*trans*-disubstituted – *cis*-disubstituted) =

$$2 \times (22 - 18) = 8 \text{ kJ/mole more stable for } \textit{trans,trans}$$

$$(2 \times (5.2 - 4.2) = 2 \text{ kcal/mole})$$

(b) gem-disubstituted – monosubstituted = 20 – 11 = 9 kJ/mole

$$(4.8 - 2.7 = 2.1 \text{ kcal/mole})$$

2-methylbut-1-ene is more stable

7-10 continued

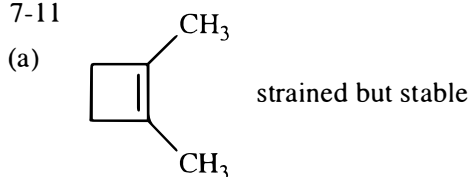
- (c) trisubstituted – *gem*-disubstituted = $25 - 20 = 5 \text{ kJ/mole}$
 $(5.9 - 4.8 = 1.1 \text{ kcal/mole})$

2-methylbut-2-ene is more stable

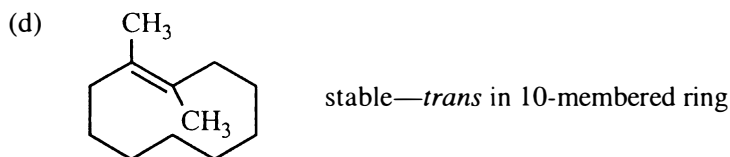
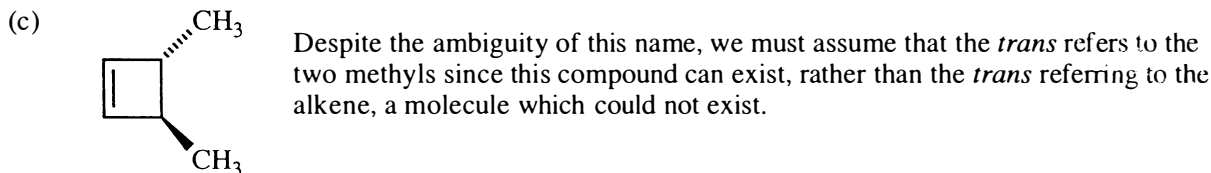
- (d) tetrasubstituted – *gem*-disubstituted = $26 - 20 = 6 \text{ kJ/mole}$
 $(6.2 - 4.8 = 1.4 \text{ kcal/mole})$

2,3-dimethylbut-2-ene is more stable

7-11



- (b) could not exist—ring size must be 8 atoms or greater to include *trans* double bond

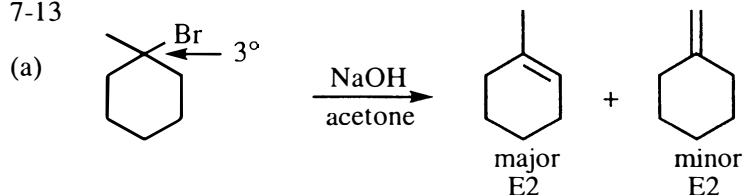


- (e) unstable at room temperature—cannot have *trans* alkene in 7-membered ring (possibly isolable at very low temperature—this type of experiment is one of the challenges chemists attack with gusto)
 (f) stable—alkene not at bridgehead
 (g) unstable—violation of Bredt's Rule (alkene at bridgehead in 6-membered ring)
 (h) stable—alkene at bridgehead in 8-membered ring
 (i) unstable—violation of Bredt's Rule (alkene at bridgehead in 7-membered ring)

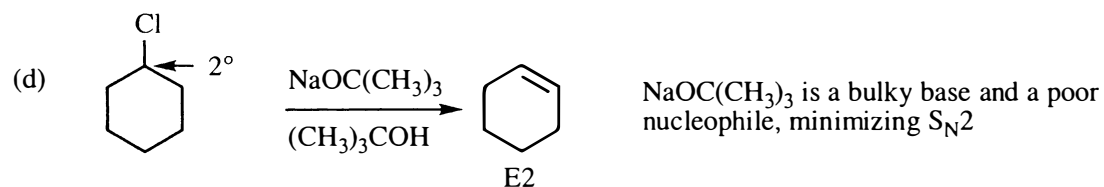
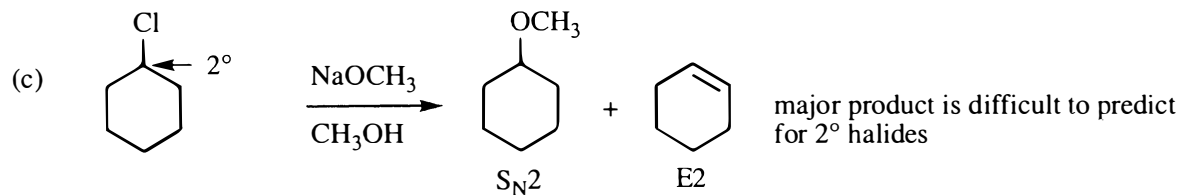
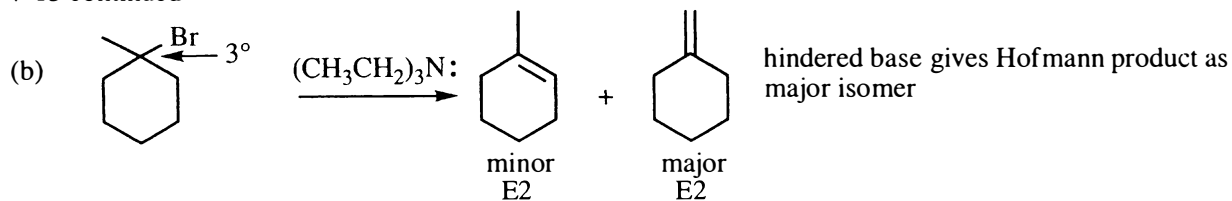
7-12

- (a) The dibromo compound should boil at a higher temperature because of its much larger molecular weight.
 (b) The *cis* should boil at a higher temperature than the *trans* as the *trans* has a zero dipole moment and therefore no dipole-dipole interactions.
 (c) 1,2-Dichlorocyclohexene should boil at a higher temperature because of its much larger molecular weight and larger dipole moment than cyclohexene.

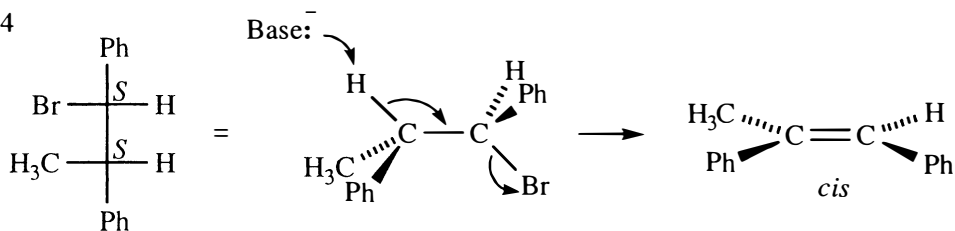
7-13



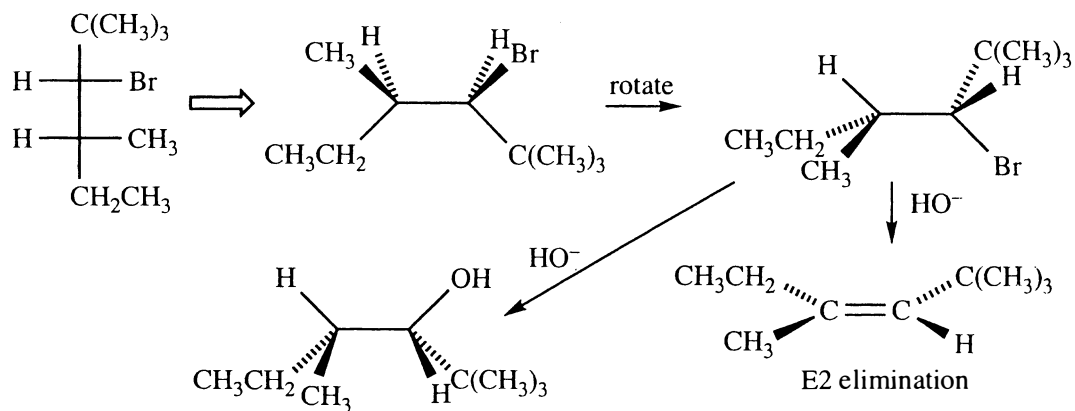
7-13 continued



7-14

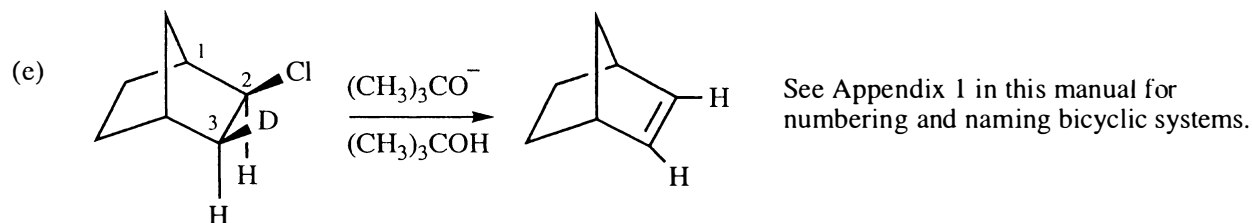
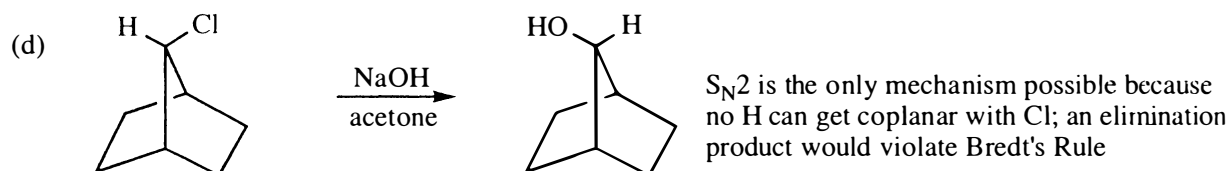
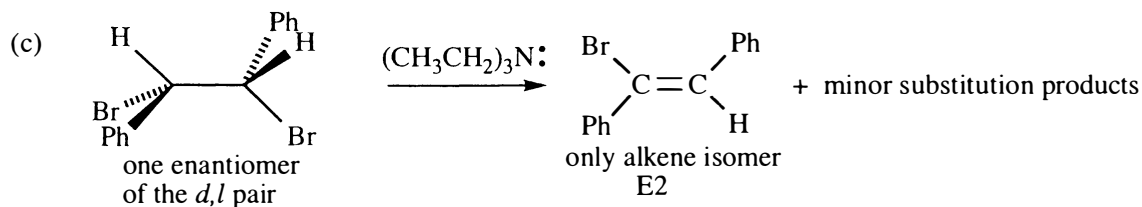
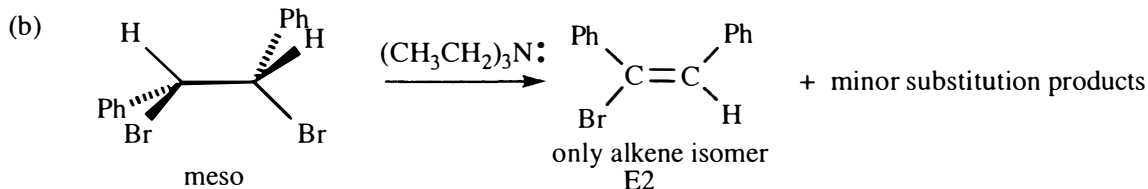


7-15 (a)



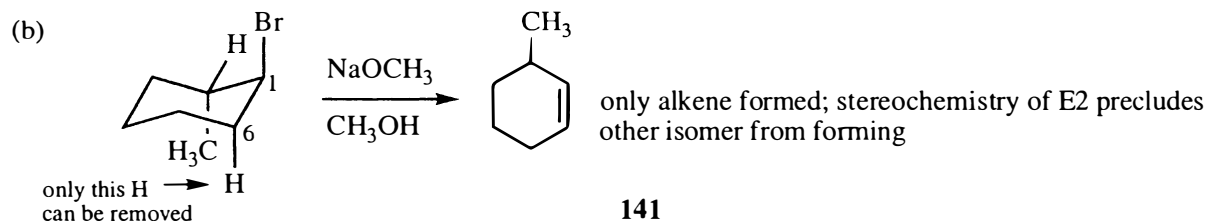
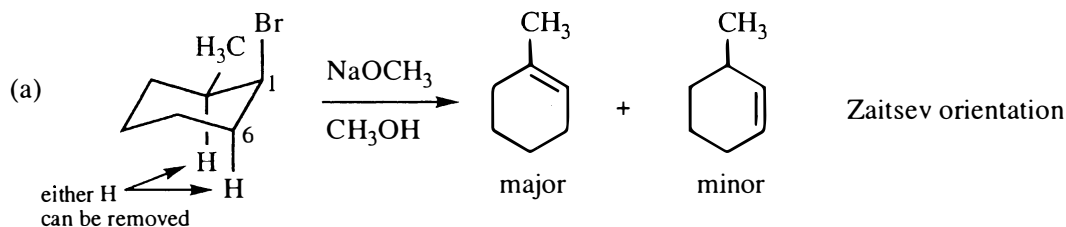
substitution product—since the substrate is a neopentyl halide and highly hindered, the S_N2 substitution is slow, and elimination is favored

7-15 continued

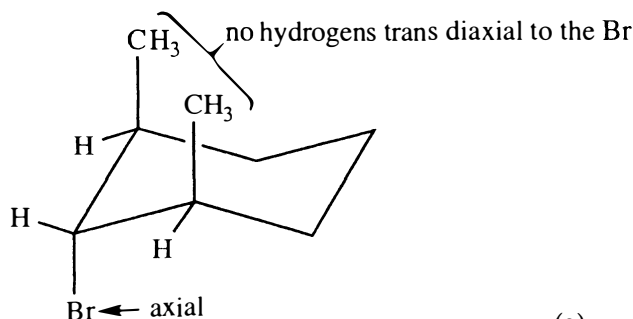


Models show that the H on C-3 cannot be anti-coplanar with the Cl on C-2. Thus, this E2 elimination must occur with a *syn*-coplanar orientation: the D must be removed as the Cl leaves.

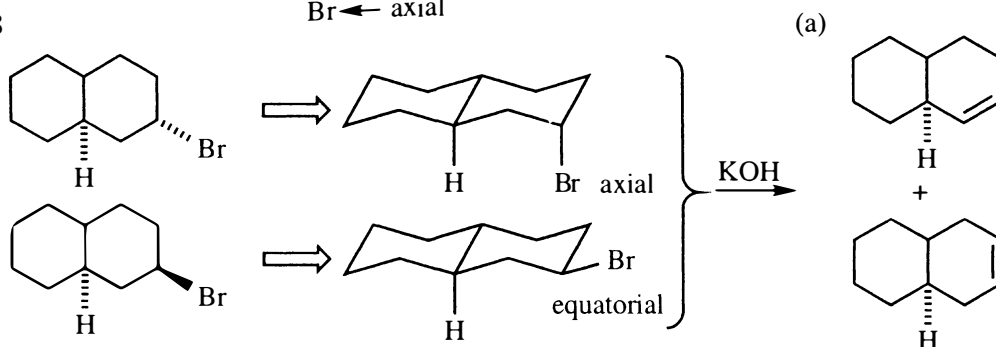
7-16 As shown in Solved Problem 7-3, the H and the Br must have trans-diaxial orientation for the E2 reaction to occur. In part (a), the *cis* isomer has the methyl in equatorial position, the NaOCH_3 can remove a hydrogen from either C-2 or C-6, giving a mixture of alkenes where the most highly substituted isomer is the major product (Zaitsev). In part (b), the *trans* isomer has the methyl in the axial position at C-2, so no elimination can occur to C-2. The only possible elimination orientation is toward C-6.



7-17 E2 elimination requires that the H and the leaving group be anti-coplanar; in a chair cyclohexane, this requires that the two groups be trans diaxial. However, when the bromine atom is in an axial position, there are no hydrogens in axial positions on adjacent carbons, so no elimination can occur.

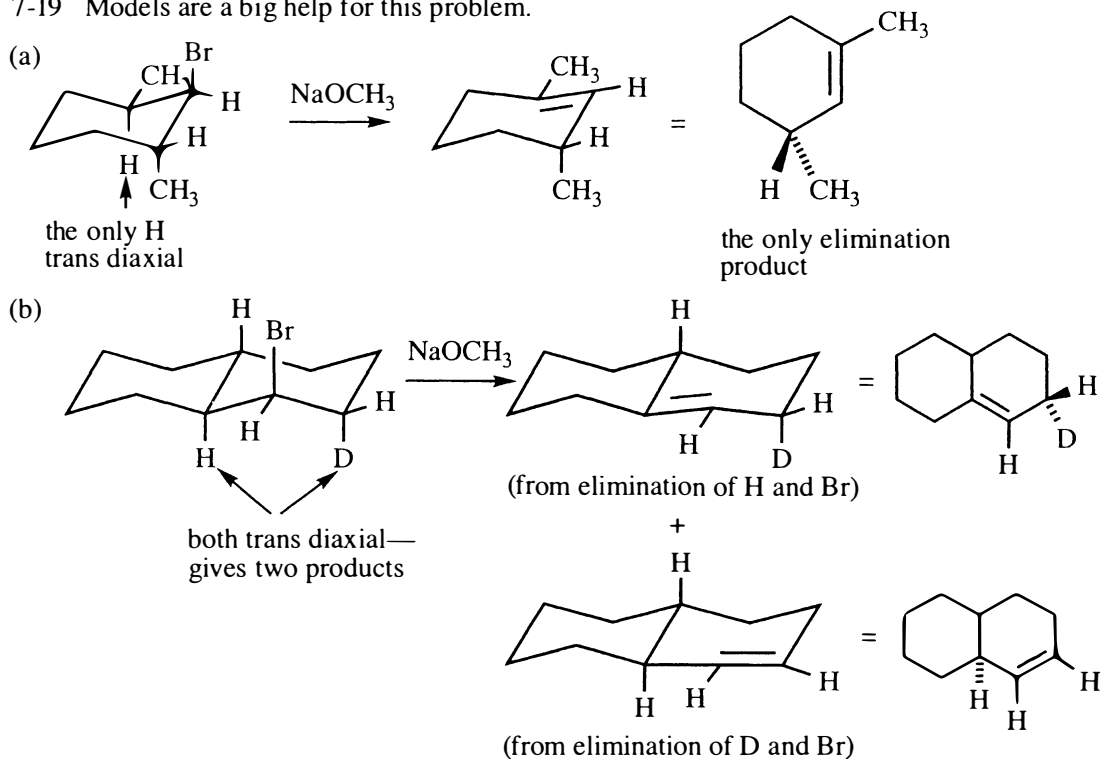


7-18

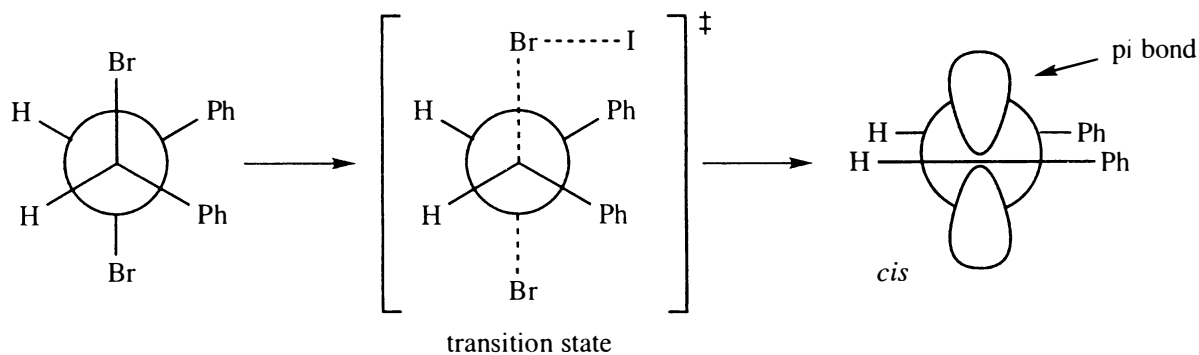
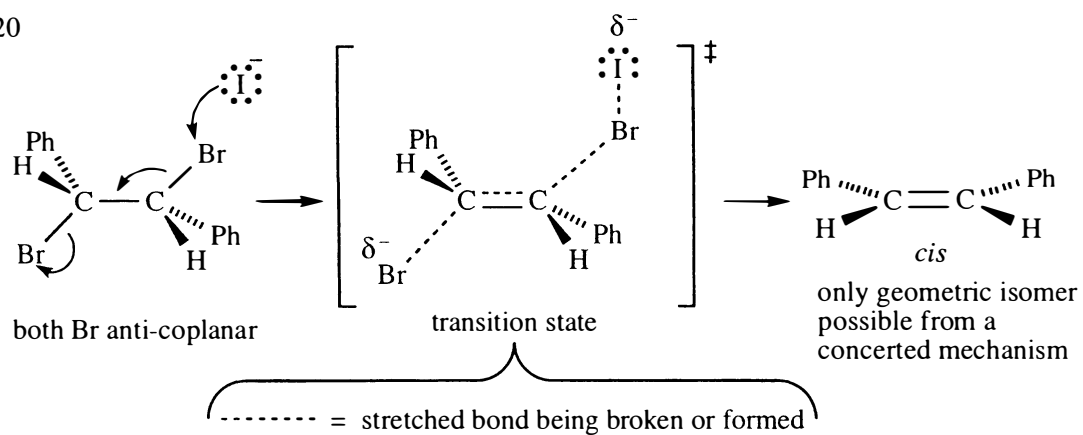


(b) Showing the chair form of the decalins makes the answer clear. The top isomer locks the H and the Br into a trans-diaxial conformation—optimum for E2 elimination. The bottom isomer has Br equatorial where it is exceedingly slow to eliminate.

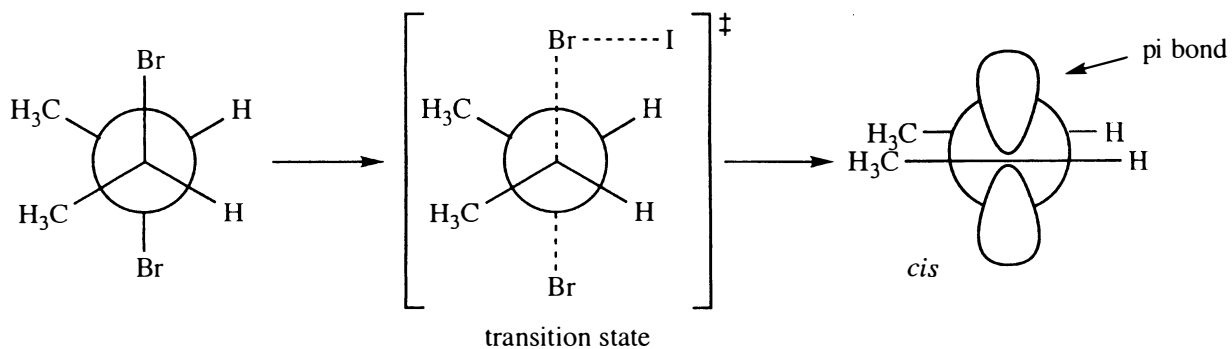
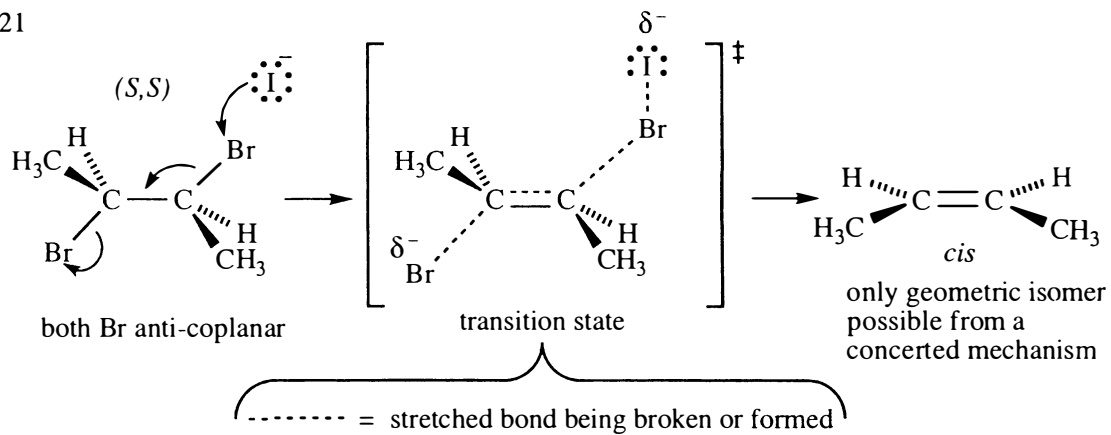
7-19 Models are a big help for this problem.



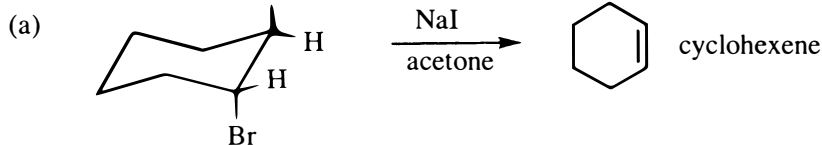
7-20



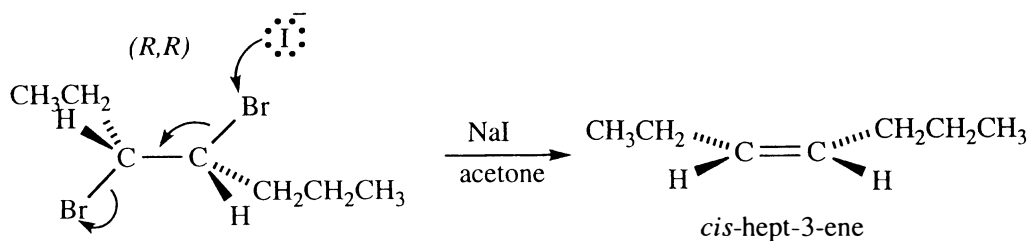
7-21



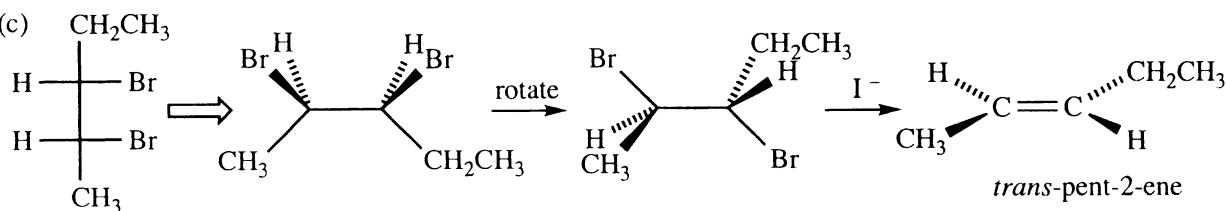
7-22



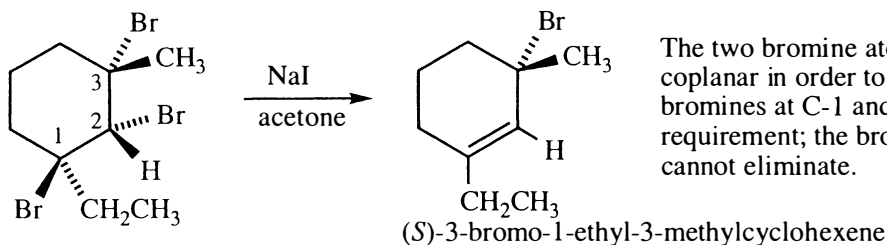
(b)



(c)

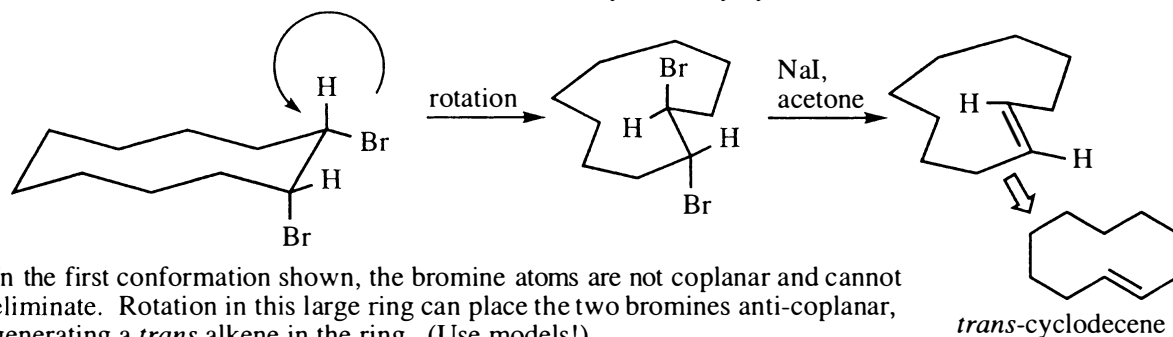


(d)



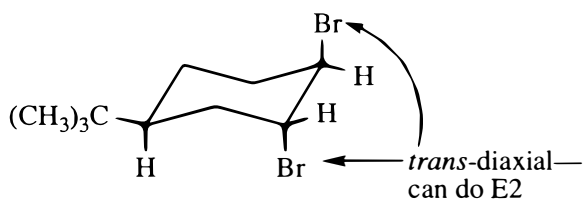
The two bromine atoms must be anti-coplanar in order to eliminate. Only the bromines at C-1 and C-2 fit that requirement; the bromines at C-2 and C-3 cannot eliminate.

(e)

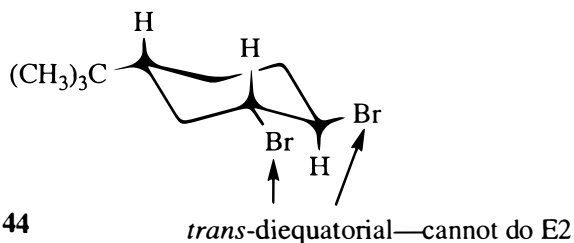


In the first conformation shown, the bromine atoms are not coplanar and cannot eliminate. Rotation in this large ring can place the two bromines anti-coplanar, generating a *trans* alkene in the ring. (Use models!)

7-23 The stereochemical requirement of E2 elimination is anti-coplanar; in cyclohexanes, this translates to *trans*-diaxial. Both dibromides are *trans*, but because the *t*-butyl group must be in an equatorial position, only the left molecule can have the bromines diaxial. The one on the right has both bromines locked into equatorial positions, from which they cannot undergo E2 elimination.

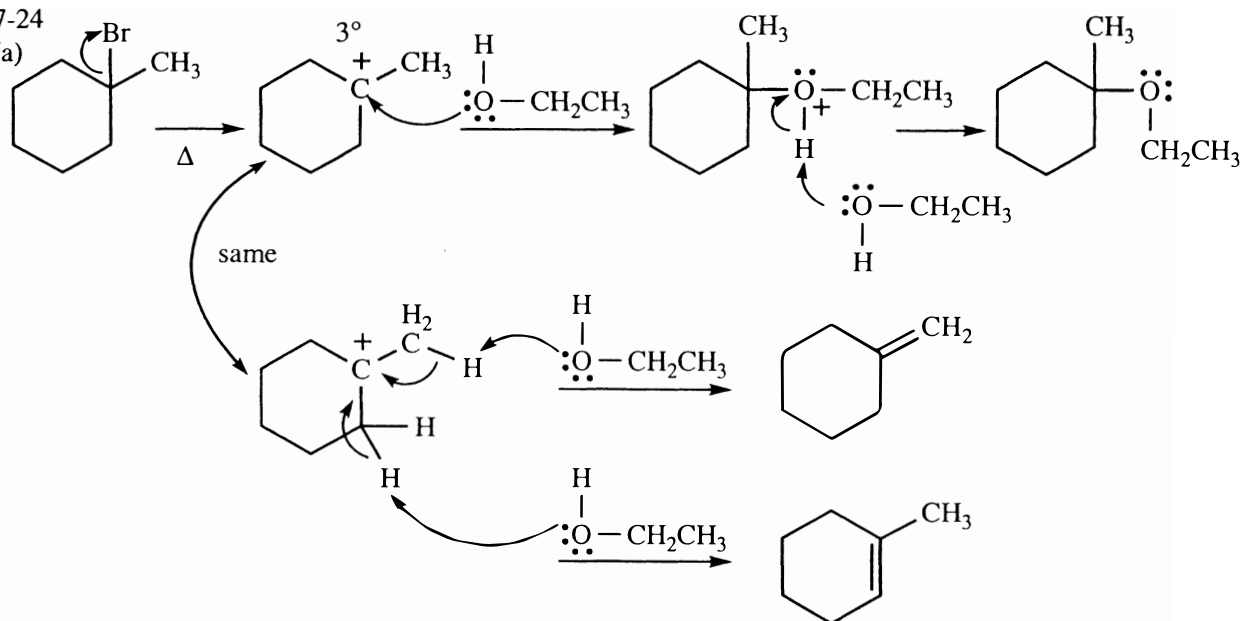


144

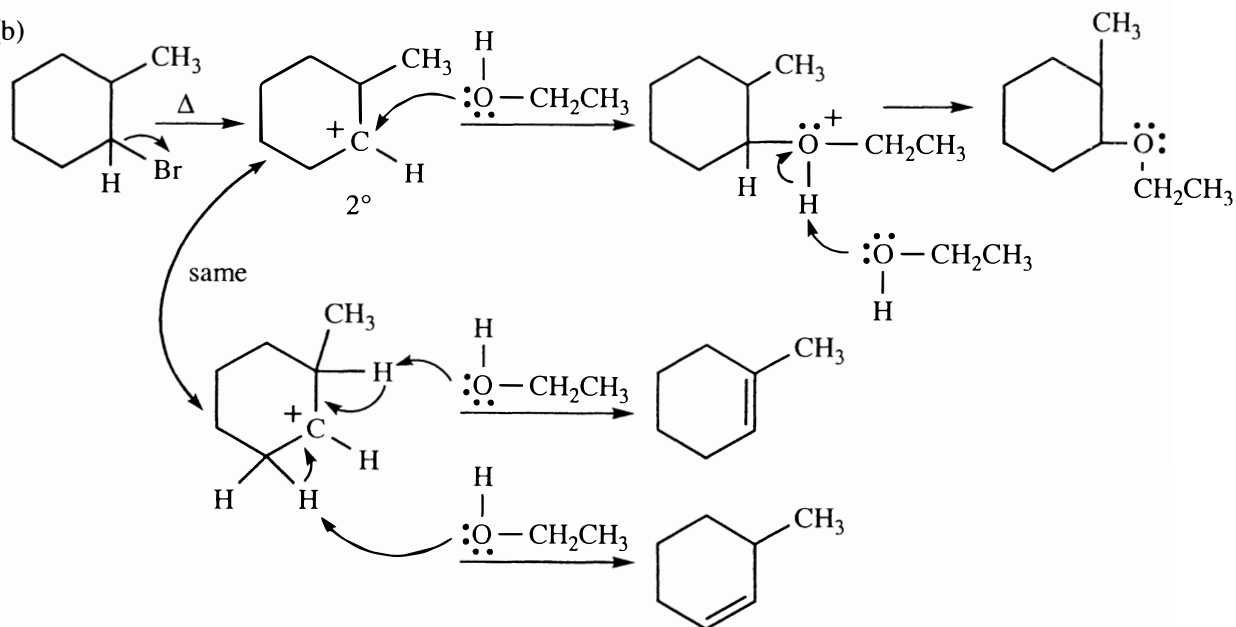
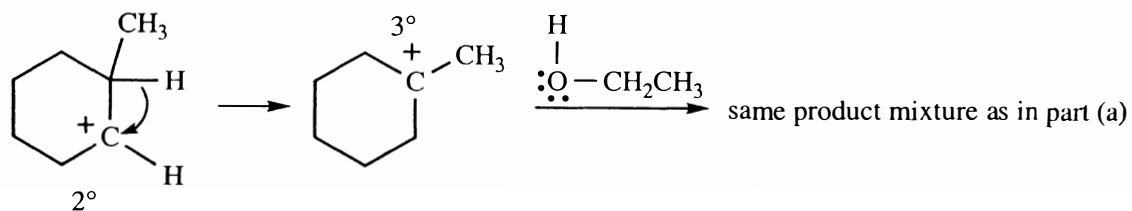


7-24

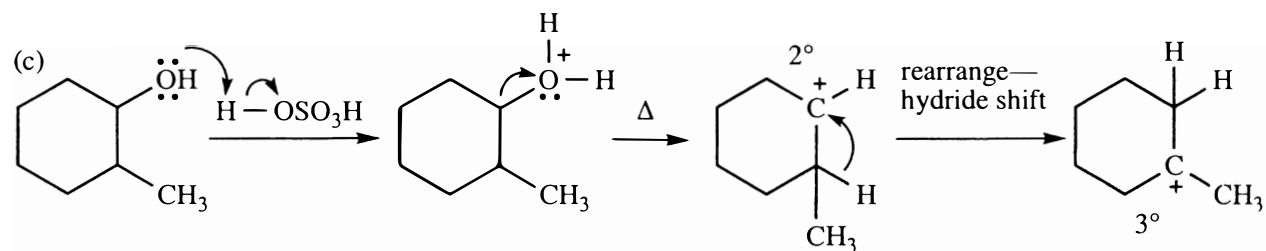
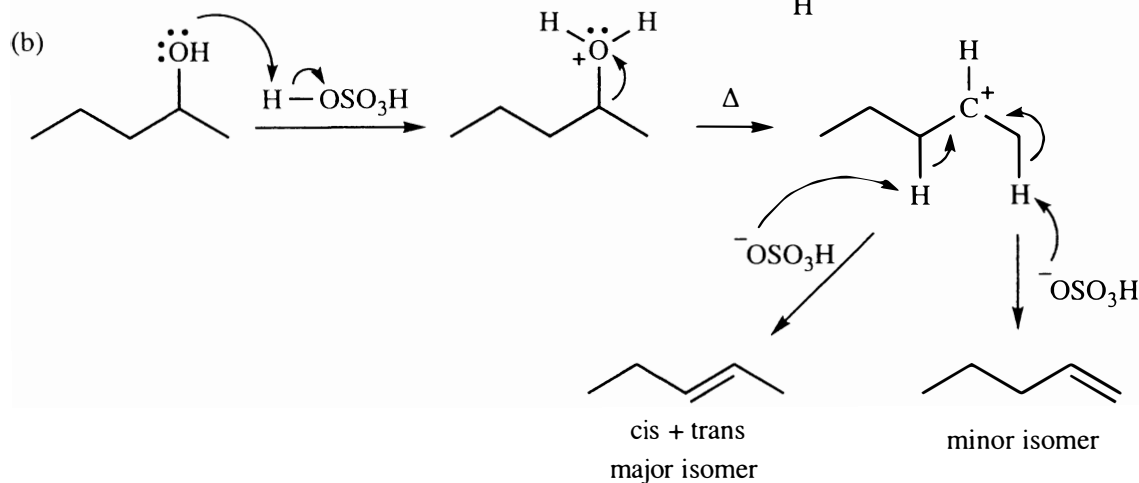
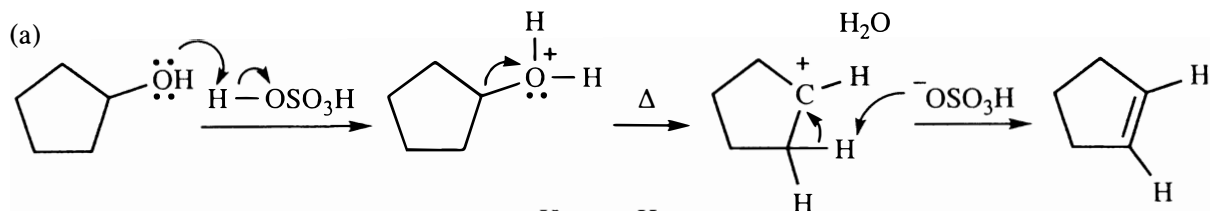
(a)



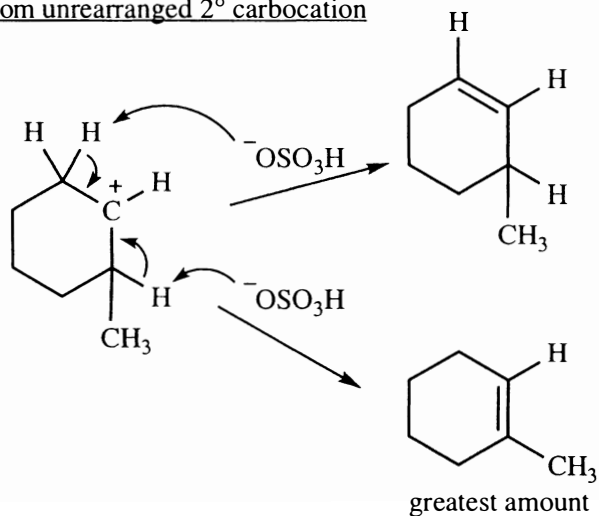
(b)

carbocation rearrangement

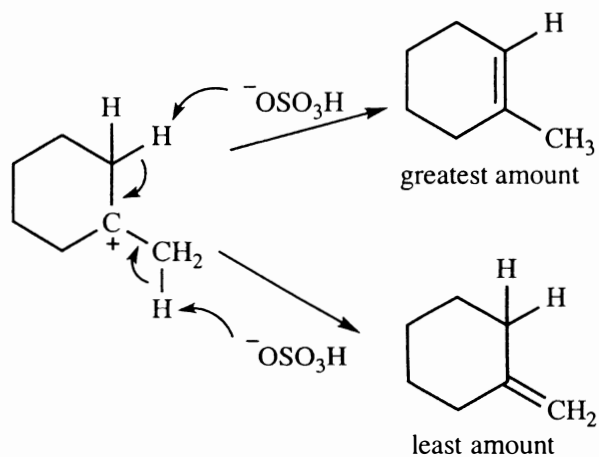
7-25 In these mechanisms, the base removing the final proton is shown as HSO_4^- . It is equally possible that water removes this proton.



from unrearranged 2° carbocation



from rearranged 3° carbocation



7-26

$$(a) \Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$$= +116,000 \text{ J/mol} - 298 \text{ K} (117 \text{ J/K}\cdot\text{mol})$$

$$= +81,100 \text{ J/mol} = +81.1 \text{ kJ/mol} (+19.3 \text{ kcal/mole})$$

ΔG° is positive, the reaction is **disfavored** at 25°C

$$(b) \Delta G_{1000} = +116,000 \text{ J/mol} - 1273 \text{ K} (117 \text{ J/K}\cdot\text{mol})$$

$$= -32,900 \text{ J/mol} = -32.9 \text{ kJ/mol} (-8.0 \text{ kcal/mole})$$

ΔG is negative, the reaction is **favored** at 1000°C

7-27

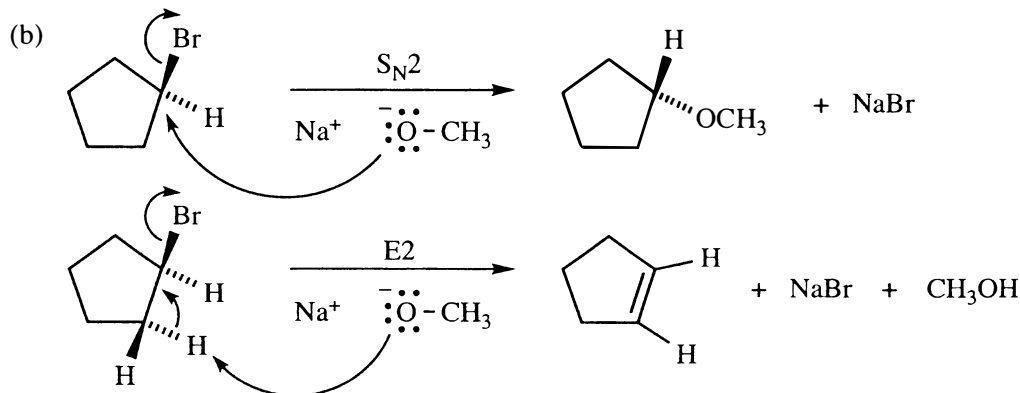
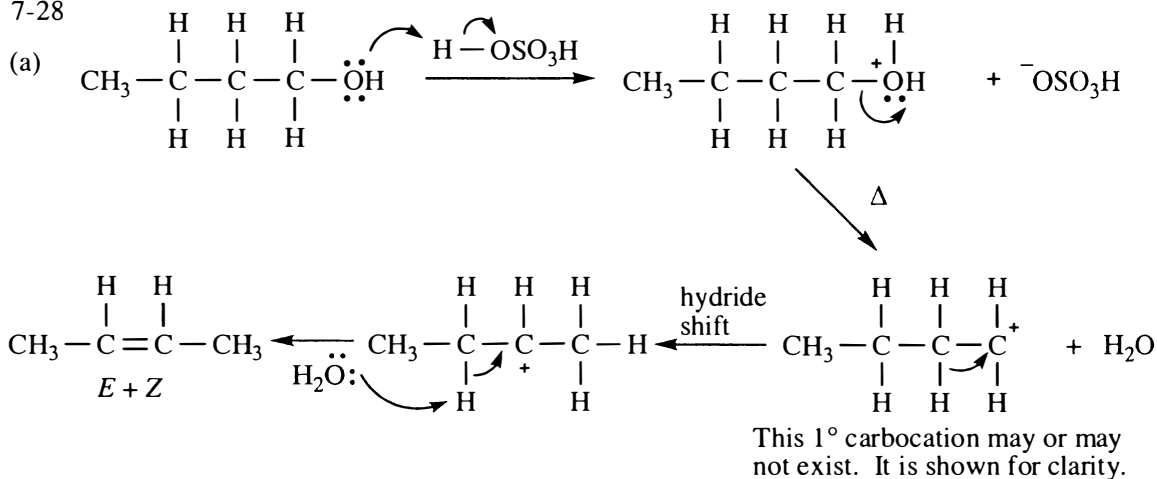
(a) basic and nucleophilic mechanism: $\text{Ba}(\text{OH})_2$ is a strong base

(b) acidic and electrophilic mechanism: the catalyst is H^+

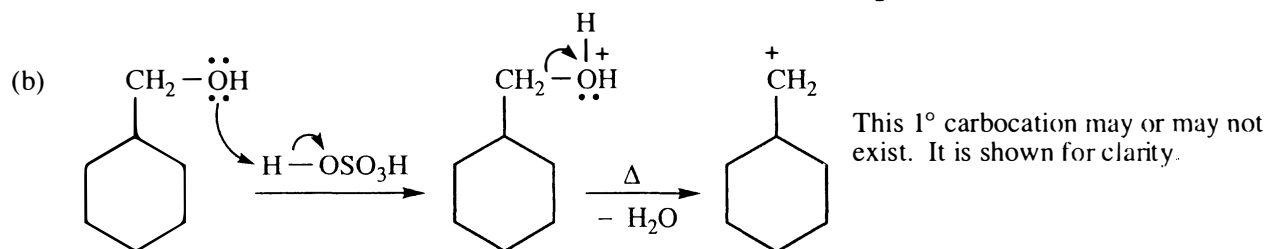
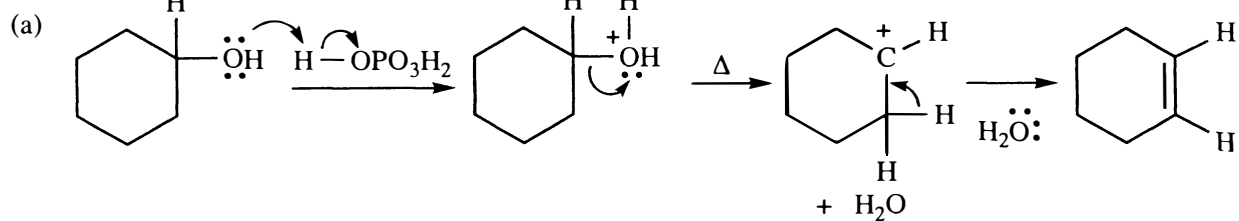
(c) free radical chain reaction: the catalyst is a peroxide that initiates free radical reactions

(d) acidic and electrophilic mechanism: the catalyst BF_3 is a strong Lewis acid

7-28

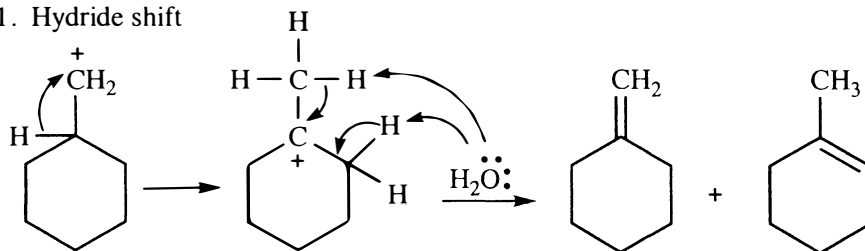


7-29

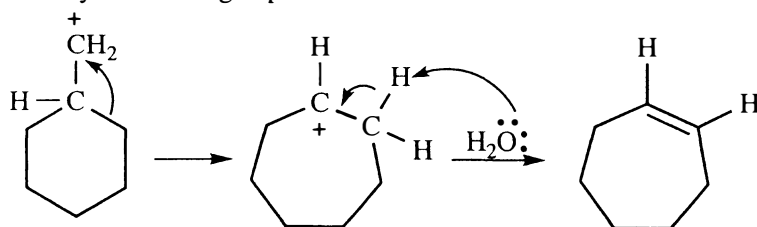


Two possible rearrangements

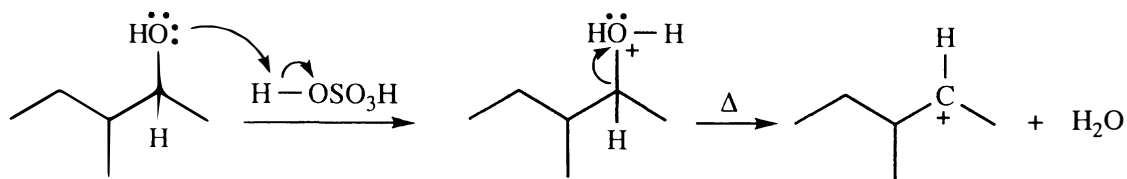
1. Hydride shift



2. Alkyl shift—ring expansion

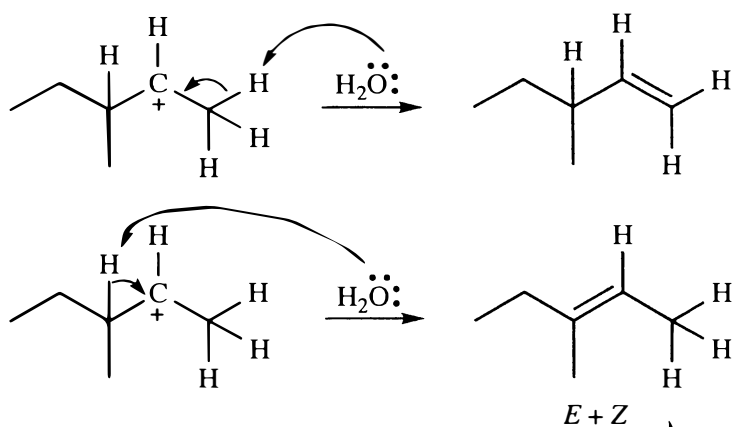


(c) carbocation formation

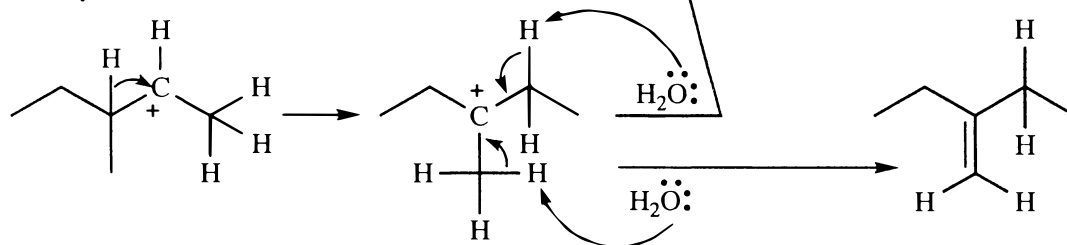


continued on next page

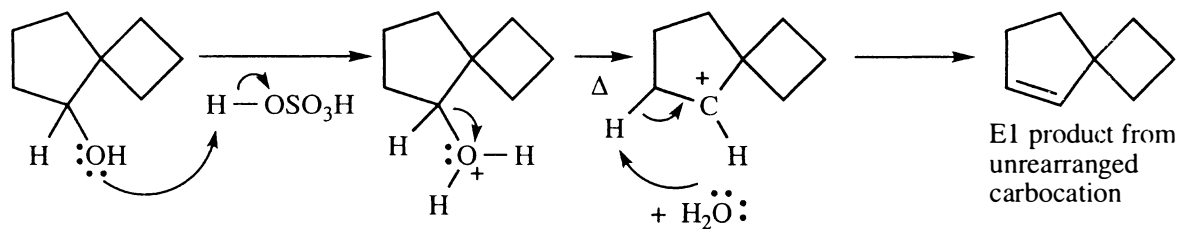
7-29 (c) continued
without rearrangement



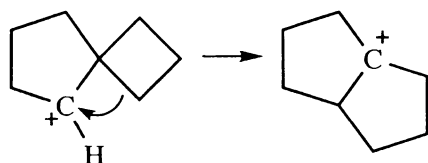
with hydride shift



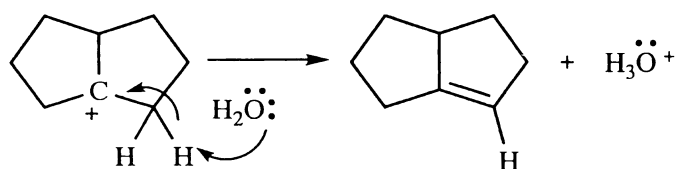
(d)



rearrangement by alkyl shift

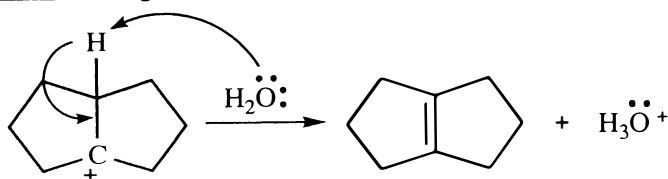


E1 on rearranged carbocation



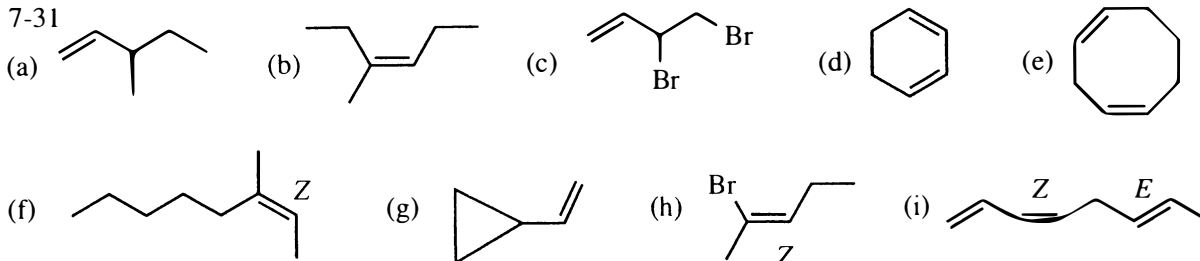
7-29 (d) continued

E1 on rearranged carbocation



7-30 Please refer to solution 1-20, page 12 of this Solutions Manual.

7-31

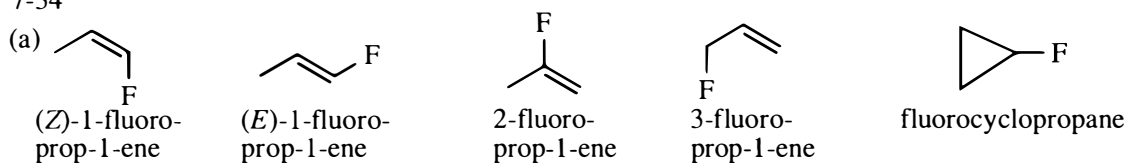


7-32

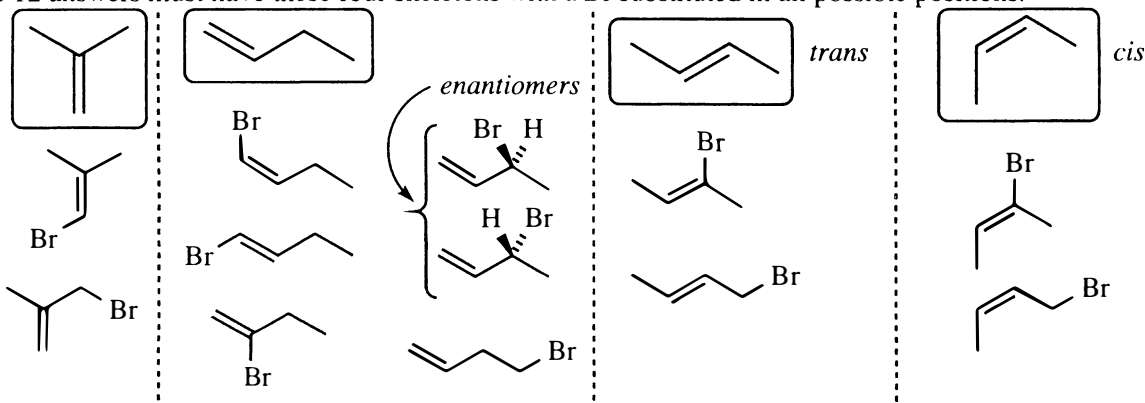
- (a) 2-ethylpent-1-ene (number the longest chain *containing the double bond*)
 (b) 3-ethylpent-2-ene
 (c) (3*E*,6*E*)-octa-1,3,6-triene
 (d) (*E*)-4-ethylhept-3-ene
 (e) 1-cyclohexylcyclohexa-1,3-diene
 (f) (3*Z*,5*E*)-6-chloro-3-(chloromethyl)octa-1,3,5-triene

7-33 (a) *E* (b) neither—two methyl groups on one carbon (c) *Z* (d) *Z*

7-34

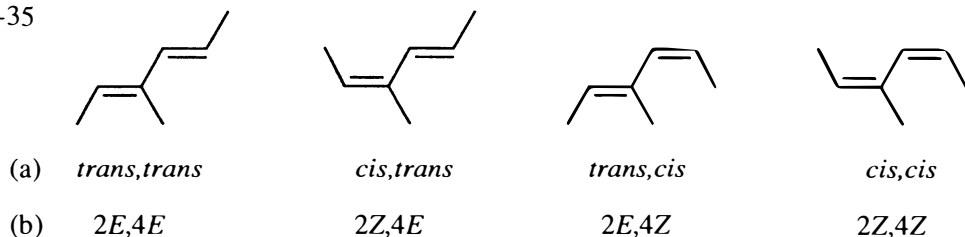


(b) C_4H_7Br has one element of unsaturation, but no rings are permitted in the problem, so all the isomers must have one double bond. Only four isomers are possible with four carbons and one double bond, so the 12 answers must have these four skeletons with a Br substituted in all possible positions.



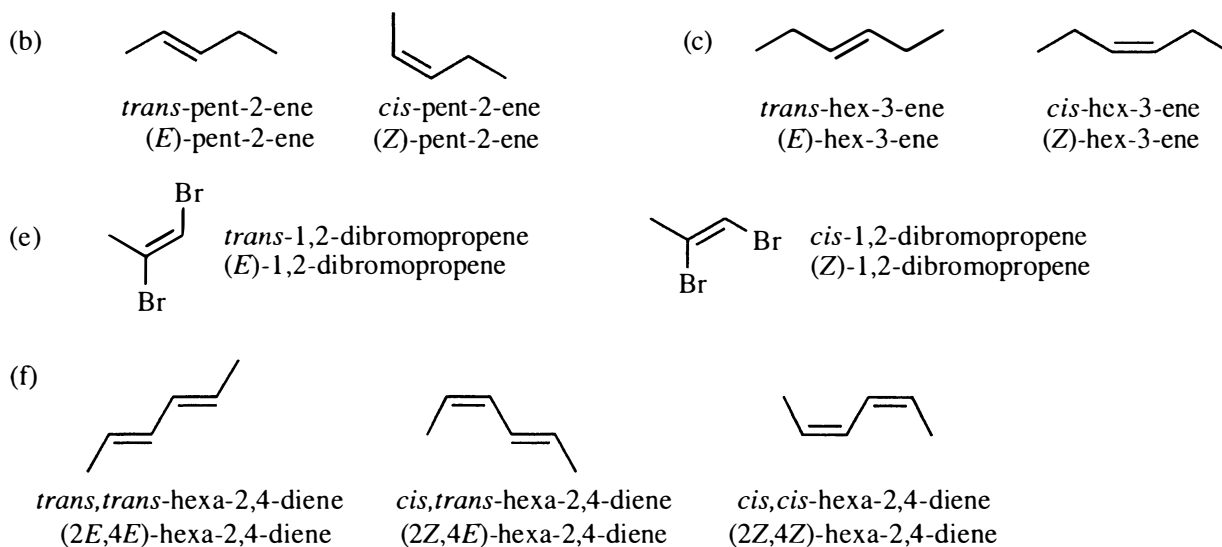
(b) Cholesterol, $C_{27}H_{46}O$, has five elements of unsaturation. If only one of those is a pi bond, the other four must be rings.

7-35

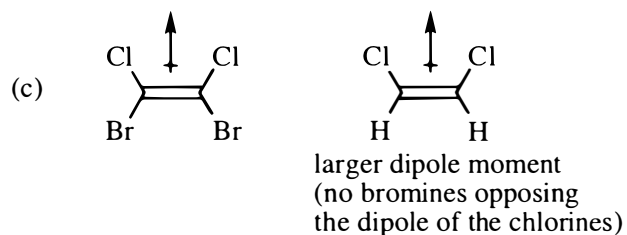
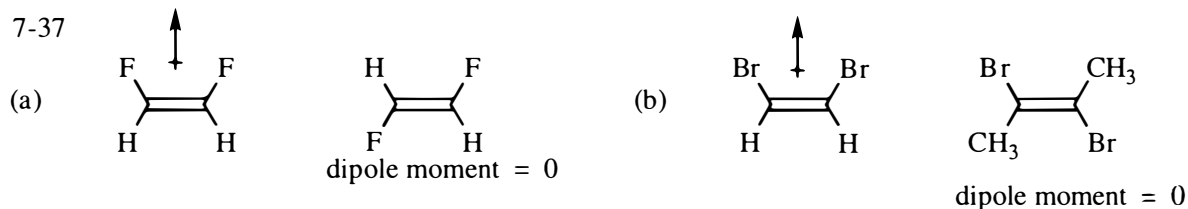


This problem is intended to show the difficulty of using *cis-trans* nomenclature with any but the simplest alkenes. *Cis* and *trans* are ambiguous: the first alkene in part (a) is *cis* if the two similar substituents are considered, but *trans* if the chain is considered. The *E-Z* nomenclature is unambiguous and is preferred for all four of these isomers.

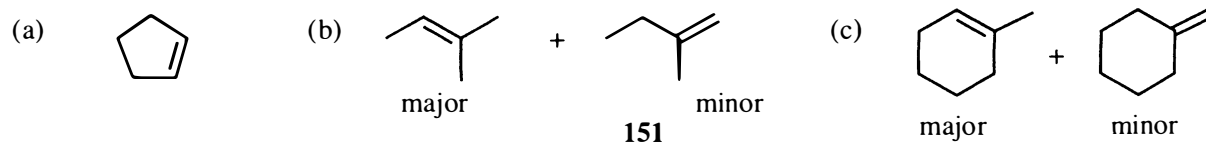
7-36 (a) and (d) have no geometric isomers



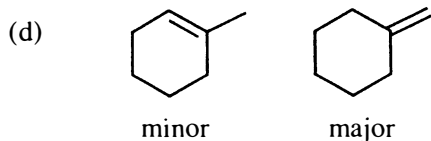
7-37



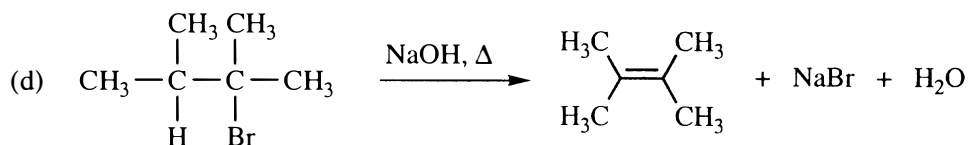
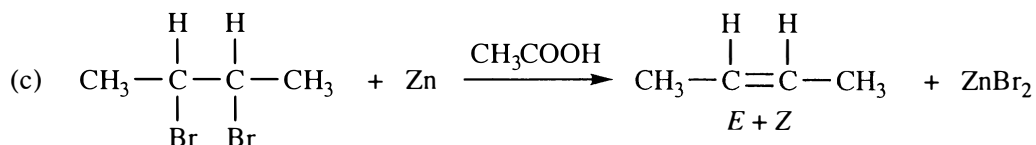
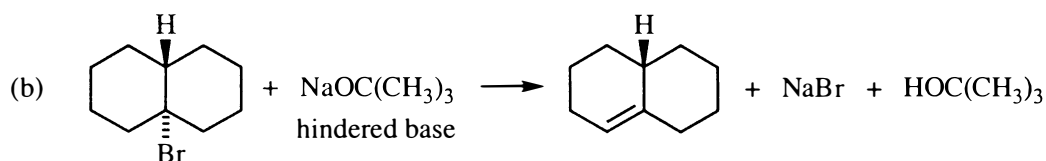
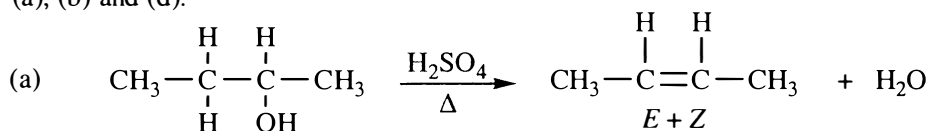
7-38



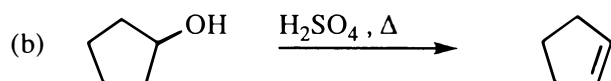
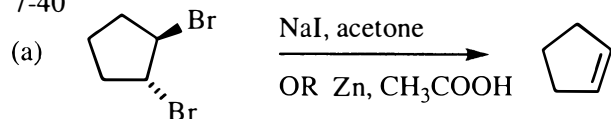
7-38 continued



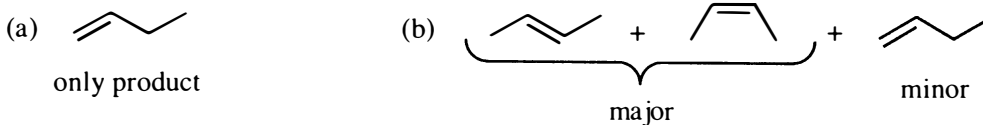
7-39 Only major alkene isomers are shown. Minor alkene isomers would also be produced in parts (a), (b) and (d).



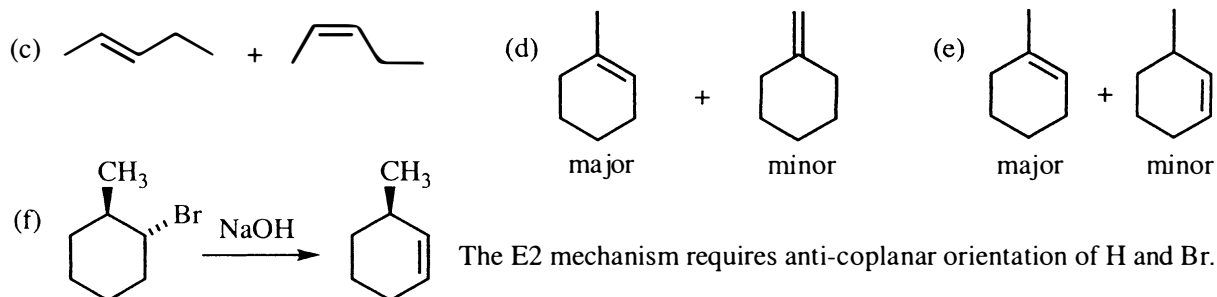
7-40



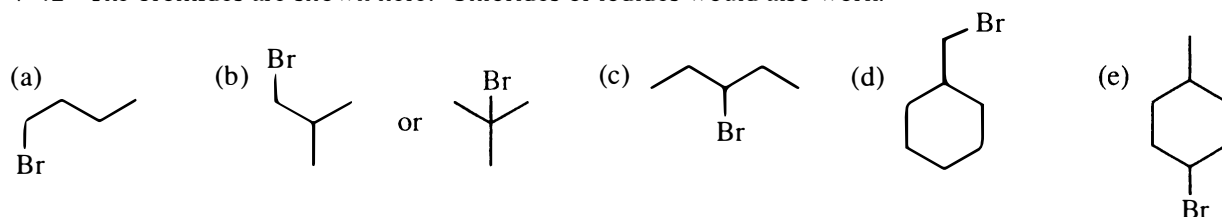
7-41



7-41 continued

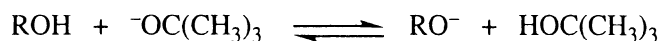


7-42 The bromides are shown here. Chlorides or iodides would also work.



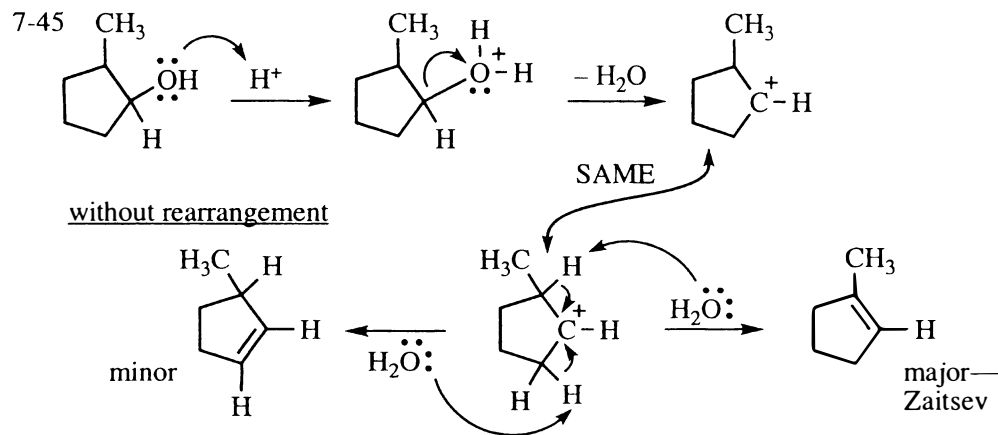
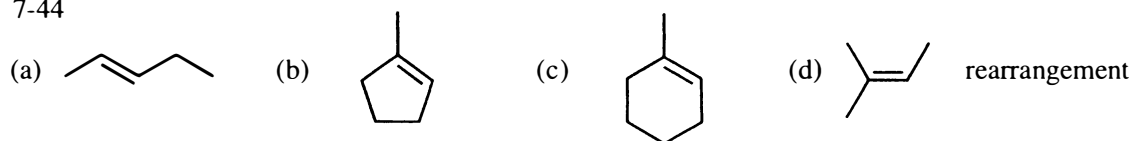
7-43

(a) There are two reasons why alcohols do not dehydrate with strong base. The potential leaving group, hydroxide, is itself a strong base and therefore a terrible leaving group. Second, the strong base deprotonates the —OH faster than any other reaction can occur, consuming the base and making the leaving group anionic and therefore even worse.

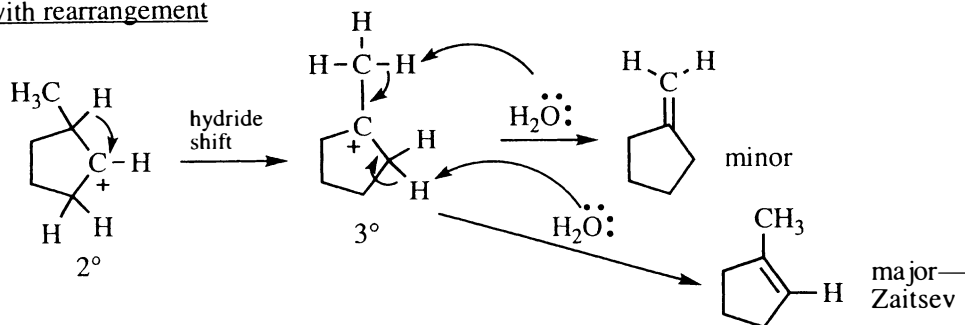


(b) A halide is already a decent leaving group. Since halides are extremely weak bases, the halogen atom is not easily protonated, and even if it were, the leaving group ability is not significantly enhanced. The hard step is to remove the adjacent H, something only a strong base can do—and strong bases will not be present under strong acid conditions.

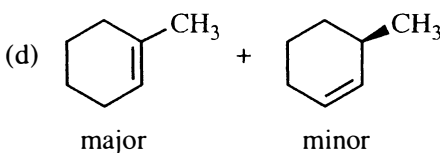
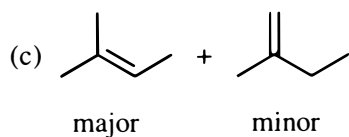
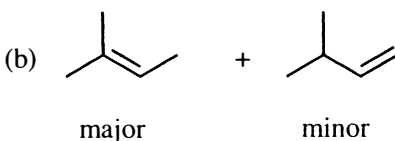
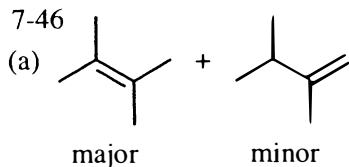
7-44



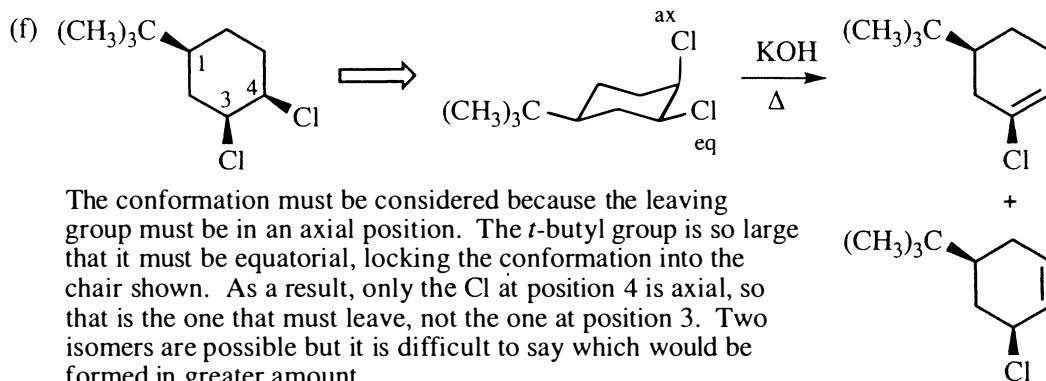
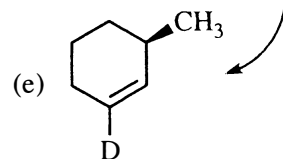
7-45 continued
with rearrangement



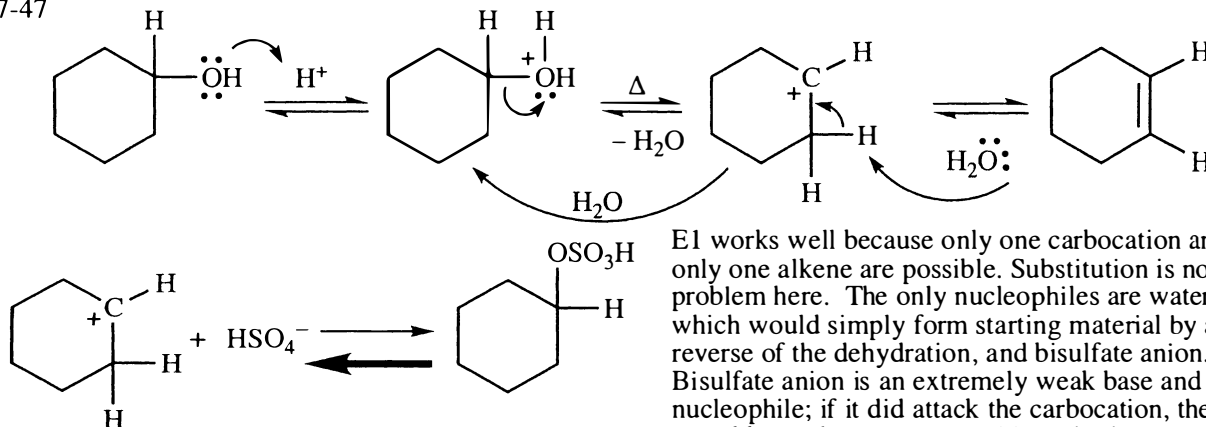
7-46



only product from E2—
anti-coplanar is
possible only from
carbon without CH₃ by
removing H and Cl



7-47



E1 works well because only one carbocation and only one alkene are possible. Substitution is not a problem here. The only nucleophiles are water, which would simply form starting material by a reverse of the dehydration, and bisulfate anion. Bisulfate anion is an extremely weak base and poor nucleophile; if it did attack the carbocation, the unstable product would quickly re-ionize, with no net change, back to the carbocation.

$$\begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{HO} \quad \text{:}\ddot{\text{O}}\text{H}
 \end{array}
 \xrightarrow{\text{H}^+}
 \begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{HO} \quad \text{:}\ddot{\text{O}}\text{H}_2^+
 \end{array}
 \xrightarrow{-\text{H}_2\text{O}}
 \begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{HO} \quad +
 \end{array}$$

The carbocation intermediate undergoes a methyl shift from C2 to C1, resulting in a more stable tertiary carbocation:

$$\begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{HO} \quad +
 \end{array}
 \xrightarrow{\text{methyl shift}}
 \begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C}^+ - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{:}\ddot{\text{O}}\text{H} \quad \text{CH}_3
 \end{array}$$

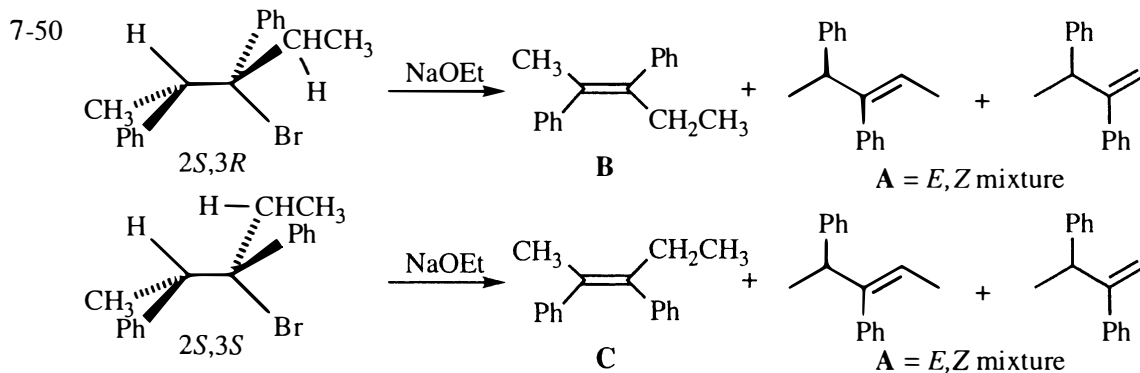
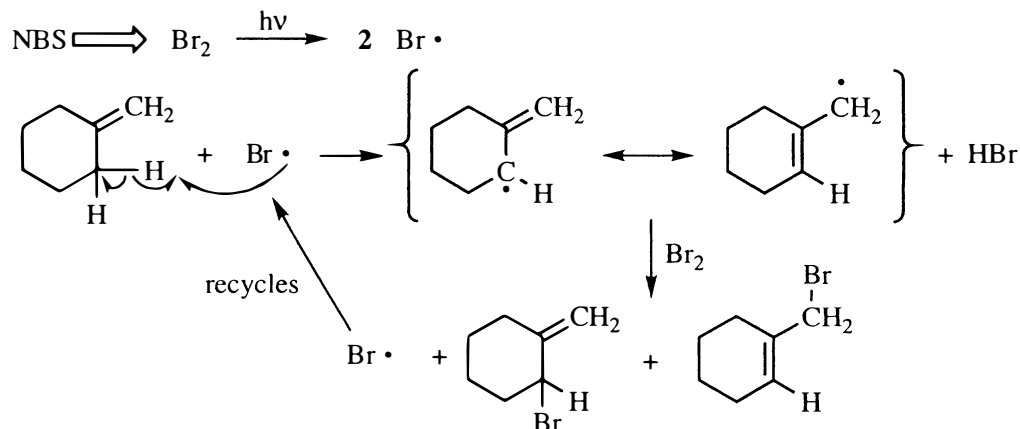
This carbocation is then attacked by a water molecule (H_2O), which acts as a nucleophile, forming a protonated alcohol intermediate:

$$\begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 || \quad | \\
 \text{:}\ddot{\text{O}}: \quad \text{CH}_3
 \end{array}
 \xleftarrow{\text{H}_2\text{O}}
 \begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 || \quad | \\
 \text{H} - \text{O}^+ \quad \text{CH}_3
 \end{array}
 \longleftrightarrow
 \begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{:}\ddot{\text{O}}\text{H}^+ \quad \text{CH}_3
 \end{array}$$

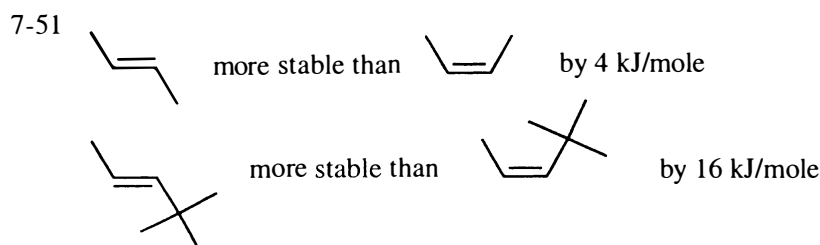
Finally, the loss of a proton (H^+) yields the neutral alcohol product, 2-methyl-2-butanol:

$$\begin{array}{c}
 \text{CH}_3 \quad \text{CH}_3 \\
 | \quad | \\
 \text{CH}_3 - \text{C} - \text{C} - \text{CH}_3 \\
 | \quad | \\
 \text{HO} \quad \text{CH}_3
 \end{array}$$

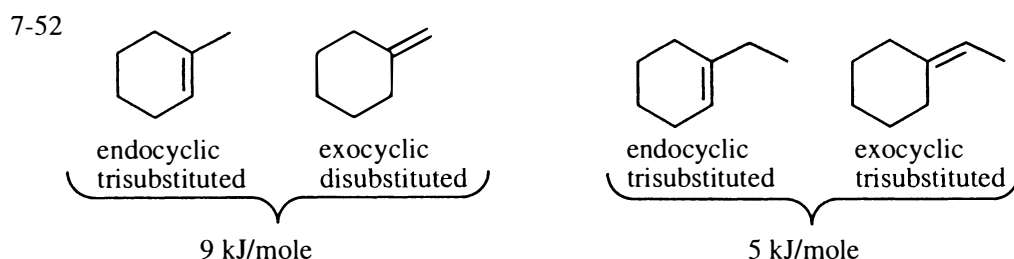
7-49 NBS generates bromine which produces bromine radical. Bromine radical abstracts an allylic hydrogen, resulting in a resonance-stabilized allylic radical. The allylic radical can bond to bromine at either of the two carbons with radical character. See the solution to problem 6-63.



155



Steric crowding by the *t*-butyl group is responsible for the energy difference. In *cis*-but-2-ene, the two methyl groups have only slight interaction. However, in the 4,4-dimethylpent-2-enes, the larger size of the *t*-butyl group crowds the methyl group in the *cis* isomer, increasing its strain and therefore its energy.



A standard principle of science is to compare experiments which differ by only one variable. Changing more than one variable clouds the interpretation, possibly to the point of invalidating the experiment.

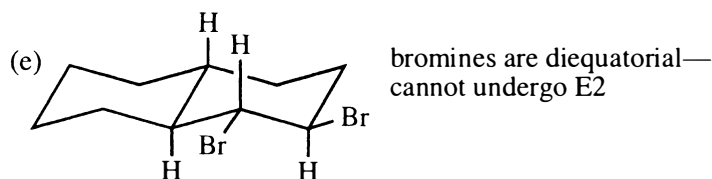
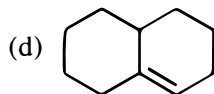
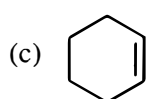
The first set of structures compares endo and exocyclic double bonds, but the degree of substitution on the alkene is also different, so this comparison is not valid—we are not isolating simply the exo or endocyclic effect.

The second pair is a much better measure of endo versus exocyclic stability because both alkenes are trisubstituted, so the degree of substitution plays no part in the energy values. Thus, 5 kJ/mole is a better value.

7-53



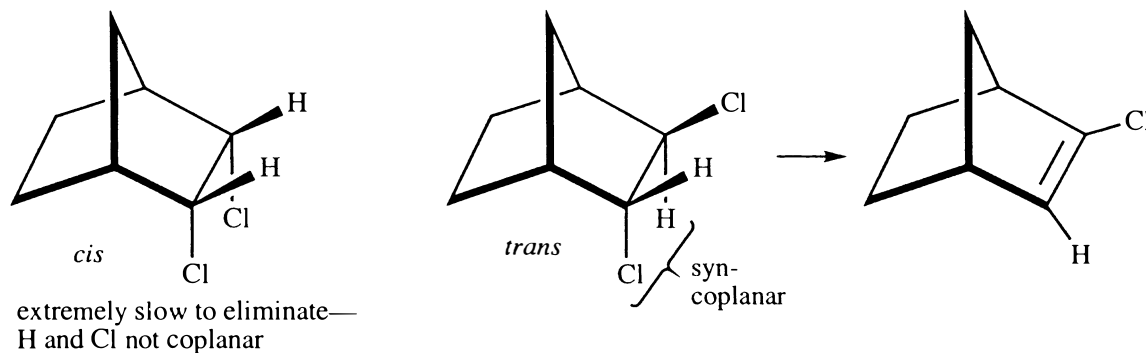
(b) No reaction—the two bromines are not trans and therefore cannot be trans-diaxial.



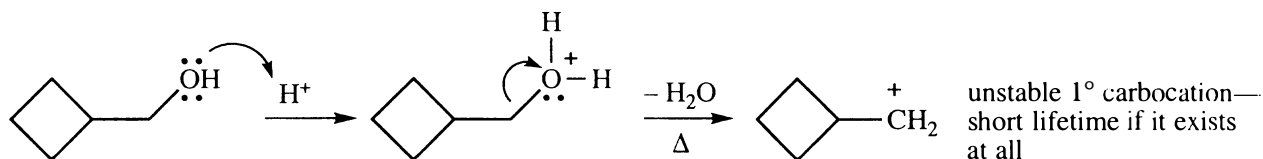
No reaction—the bromines are trans, but they are diequatorial because of the locked conformation of the trans-decalin system. E2 can occur only when the bromines are trans diaxial.

7-54 In E2, the two groups to be eliminated must be coplanar. In conformationally mobile systems like acyclic molecules, or in cyclohexanes, anti-coplanar is the preferred orientation where the H and leaving group are 180° apart. In rigid systems like norbornanes, however, SYN-coplanar (angle 0°) is the only possible orientation and E2 will occur, although at a slower rate than anti-coplanar.

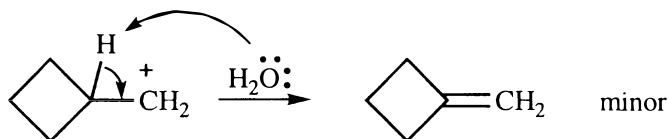
The structure having the H and the Cl syn-coplanar is the *trans*, which undergoes the E2 elimination. (It is possible that the *other* H and Cl eliminate from the *trans* isomer; the results from this reaction cannot distinguish between these two possibilities.)



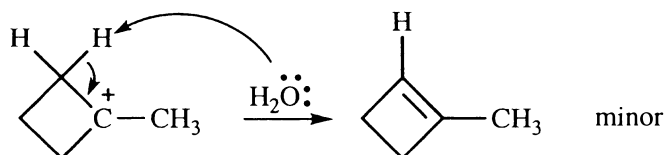
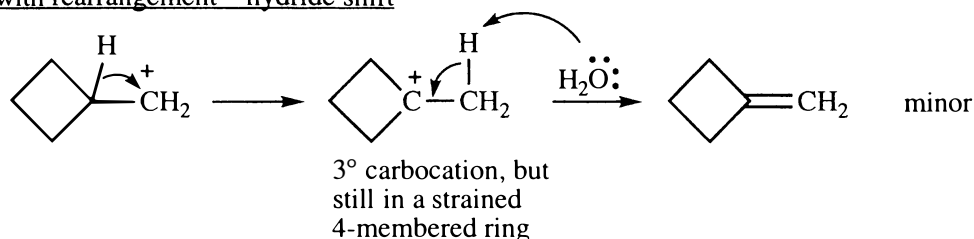
7-55 It is interesting to note that even though three-membered rings are more strained than four-membered rings, three-membered rings are far more common in nature than four-membered rings. Rearrangement from a four-membered ring to something else, especially a larger ring, will happen quickly.



without rearrangement

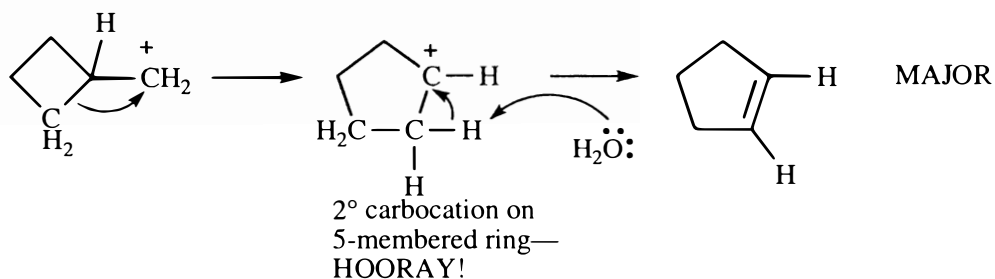


with rearrangement—hydride shift

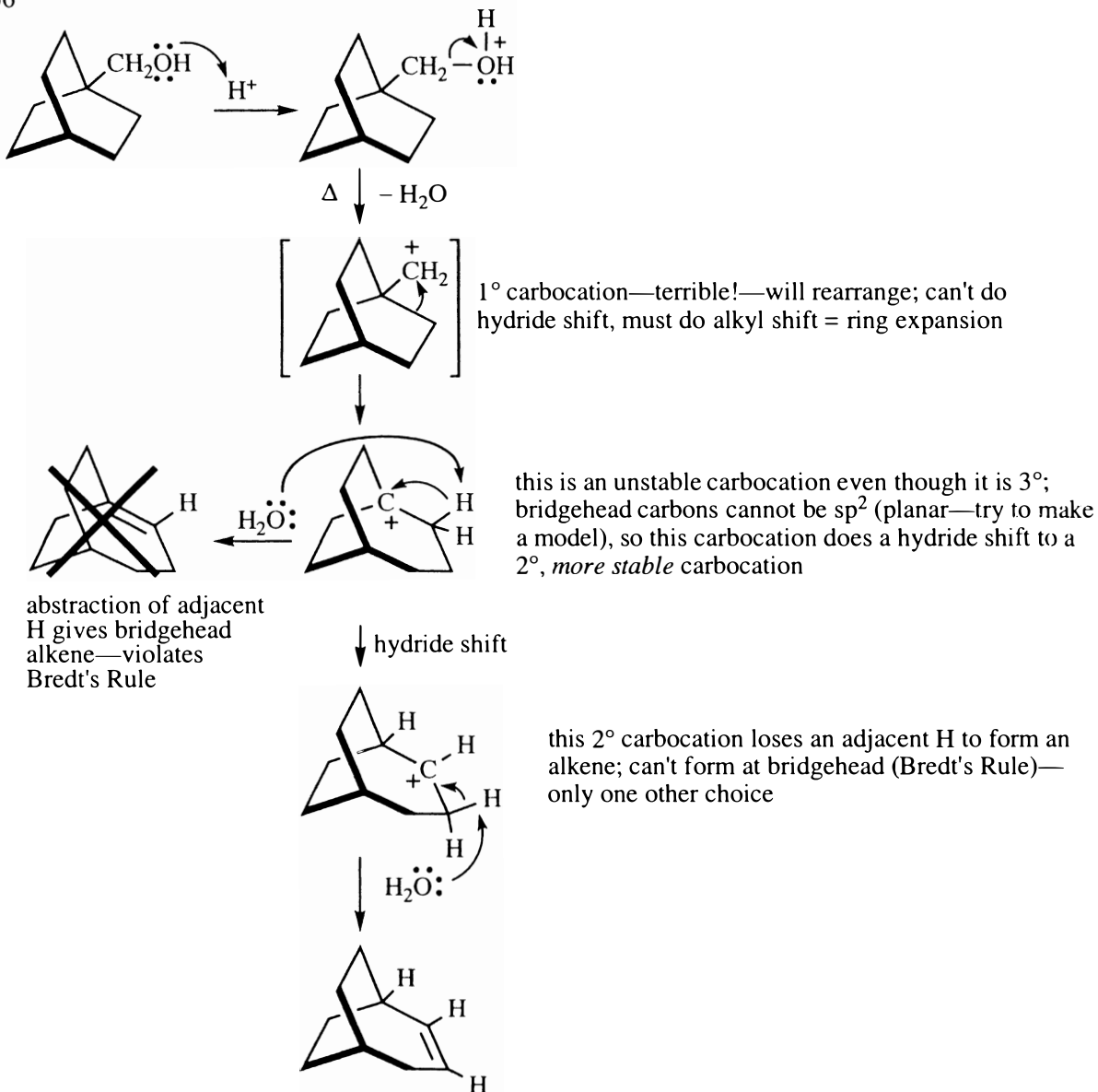


7-55 continued

with rearrangement—alkyl shift—ring expansion

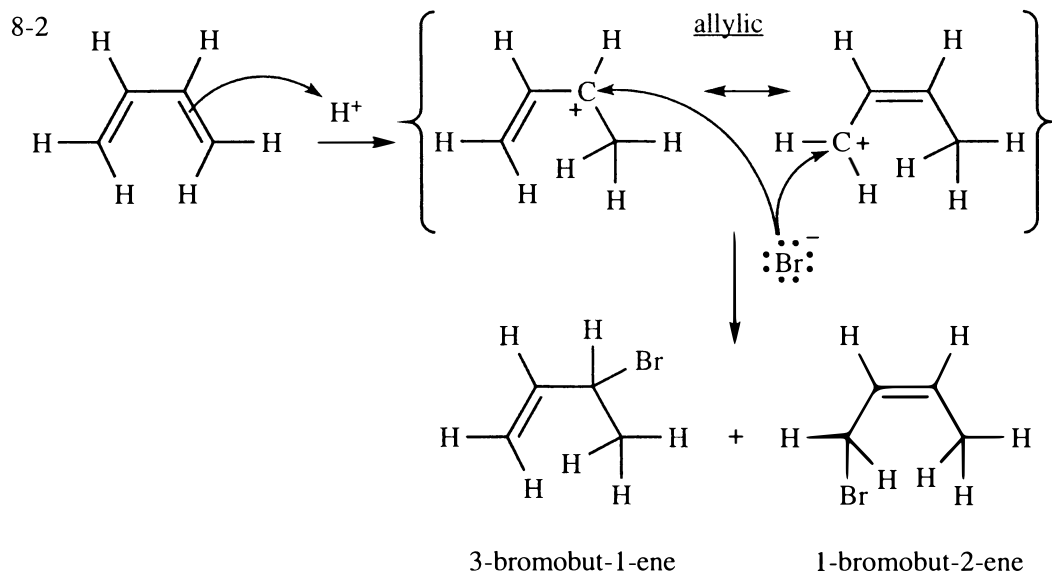
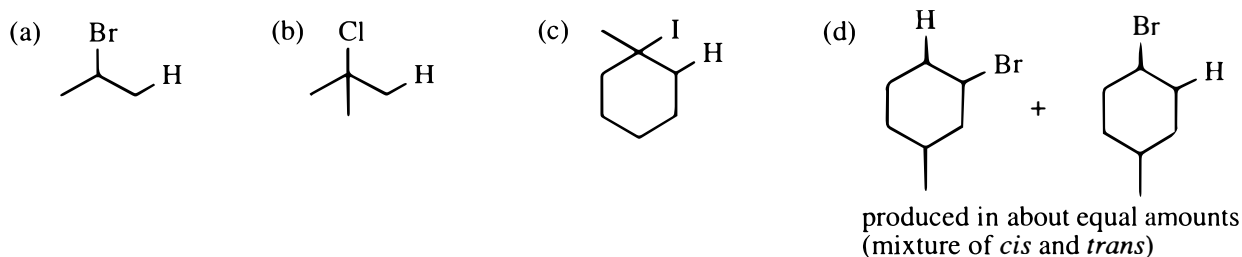


7-56

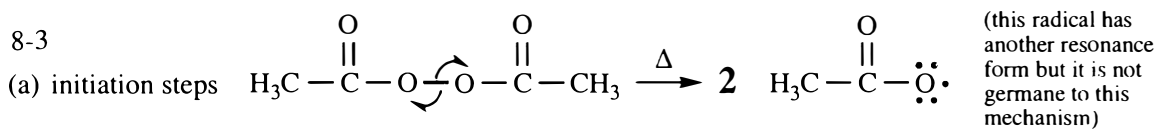


CHAPTER 8—REACTIONS OF ALKENES

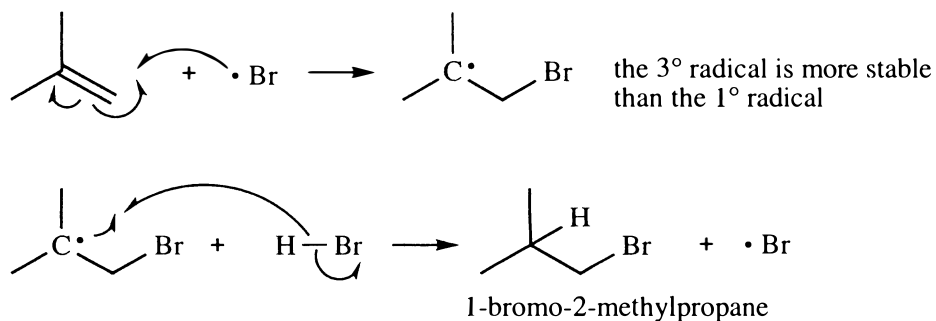
8-1 *Major* products are produced in greatest amount; they are not necessarily the *only* products produced.



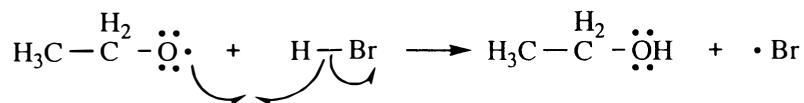
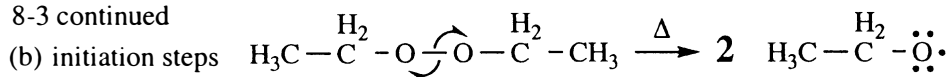
Because the allylic carbocation has partial positive charge at two carbons, the bromide nucleophile can bond at either electrophilic carbon, giving two products.



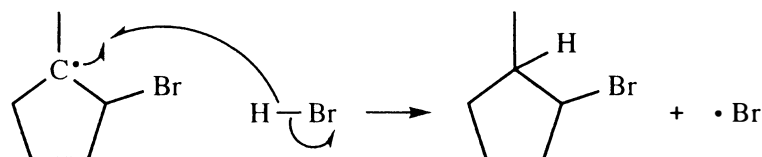
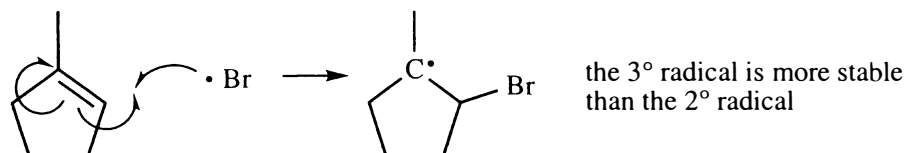
propagation steps



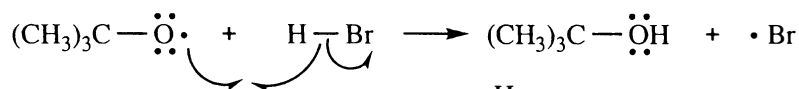
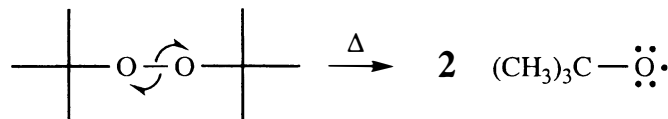
8-3 continued



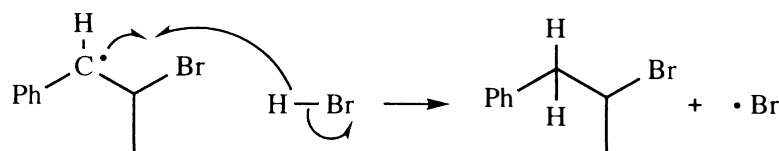
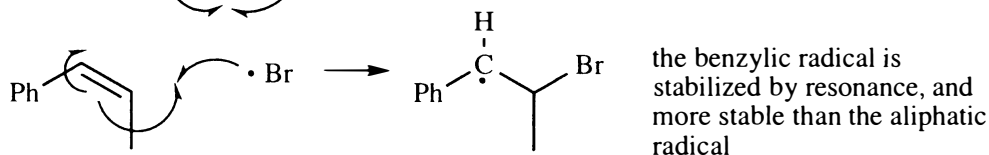
propagation steps

1-bromo-2-methylcyclopentane (*cis* + *trans*)

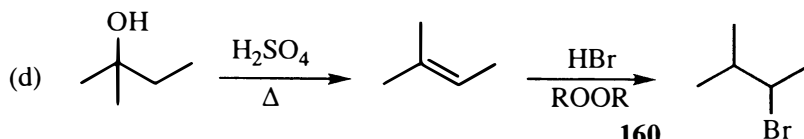
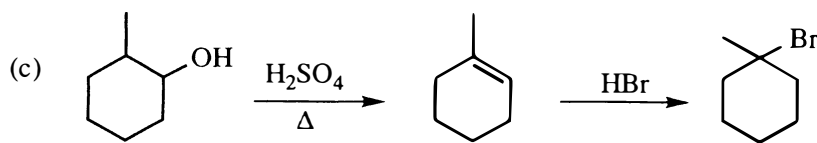
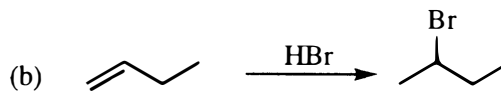
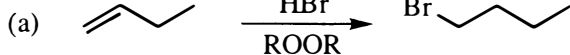
(c) initiation steps



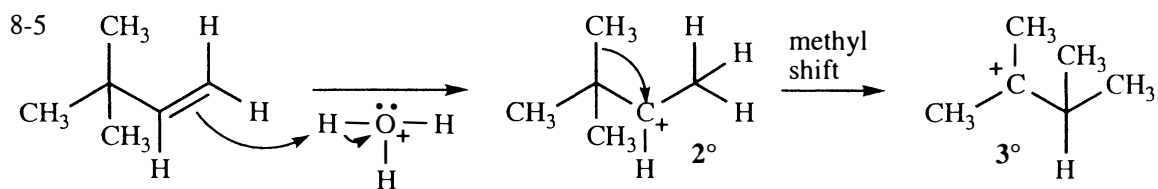
propagation steps

2-bromo-1-phenylpropane
(recall that "Ph" is the abbreviation for "phenyl")

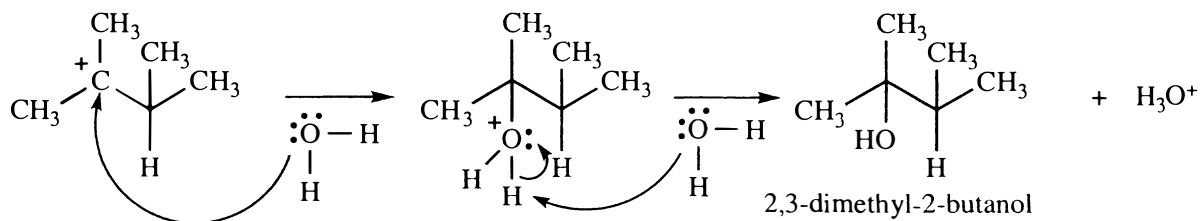
8-4



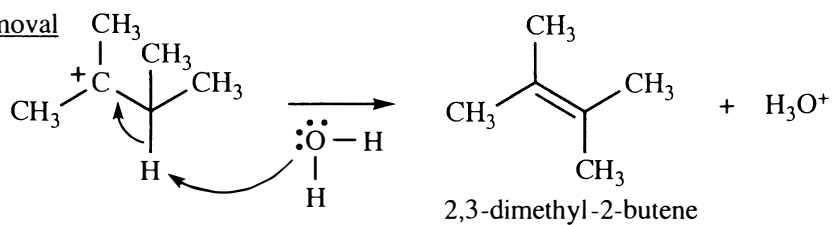
Note: A good synthesis uses major products as intermediates, not minor products. Knowing orientation of addition and elimination is critical to using reactions correctly.



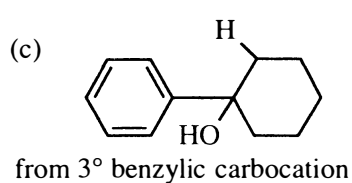
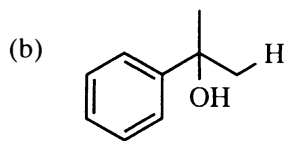
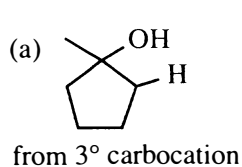
nucleophilic attack by water



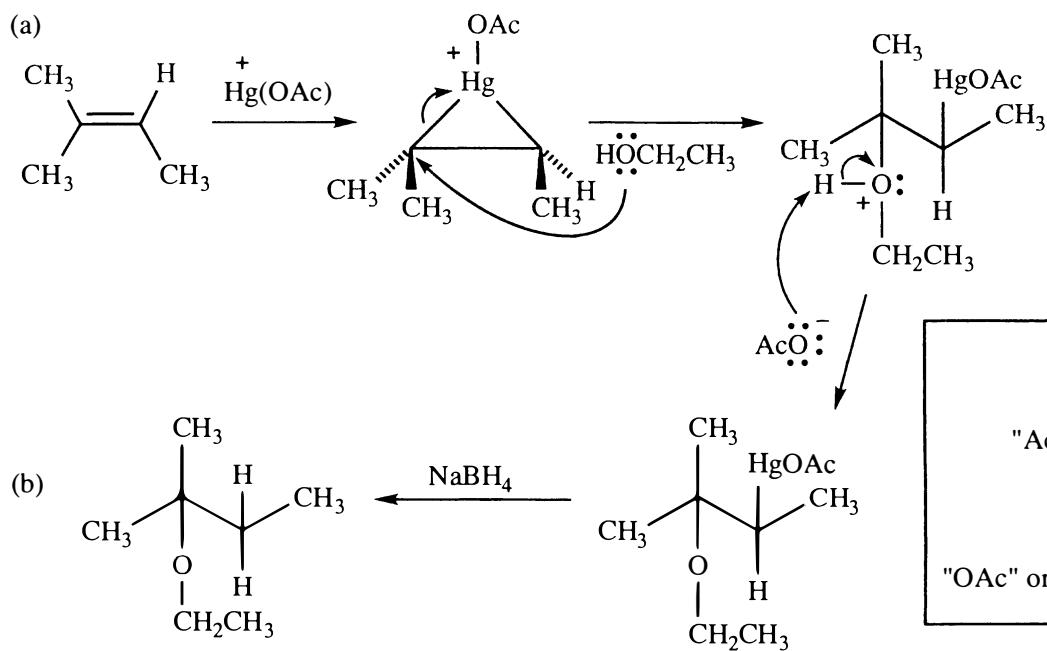
proton removal



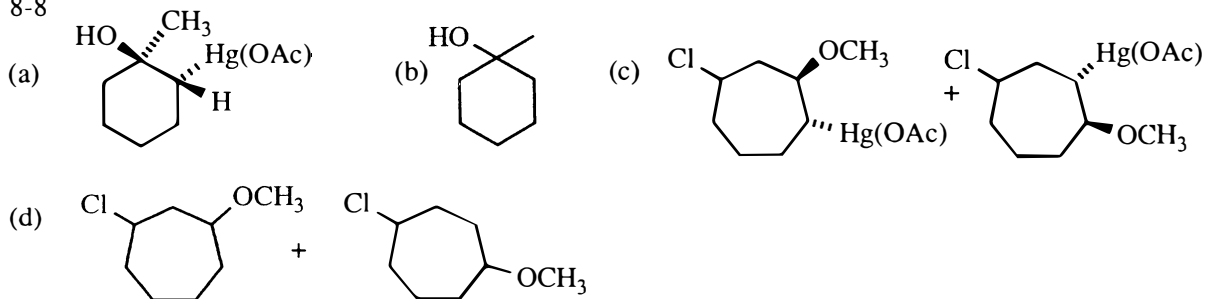
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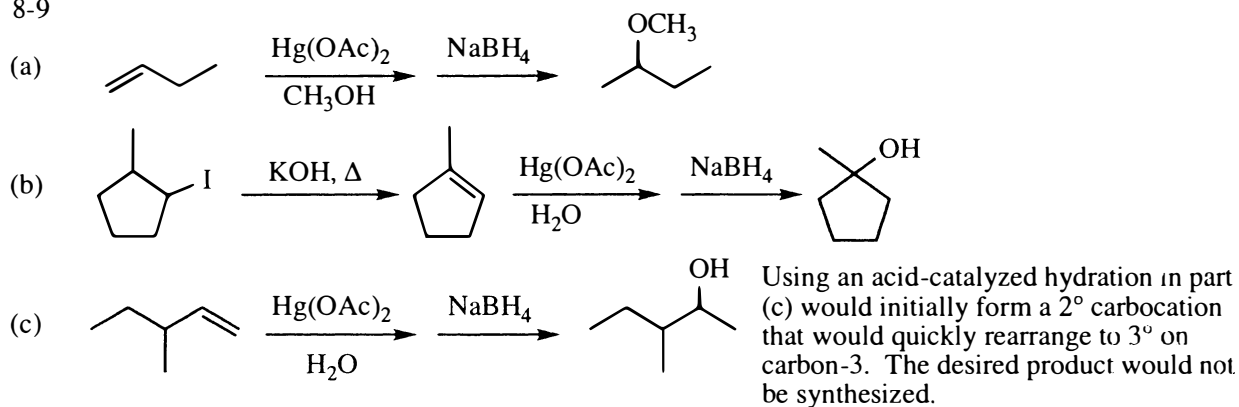
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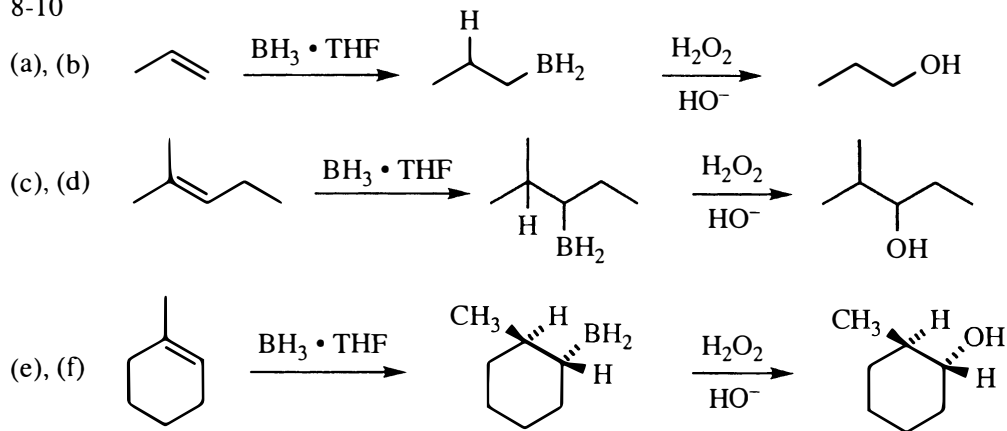
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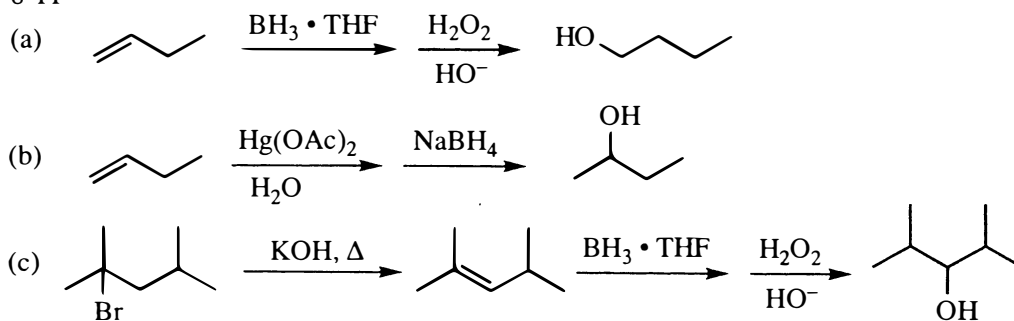
8-9



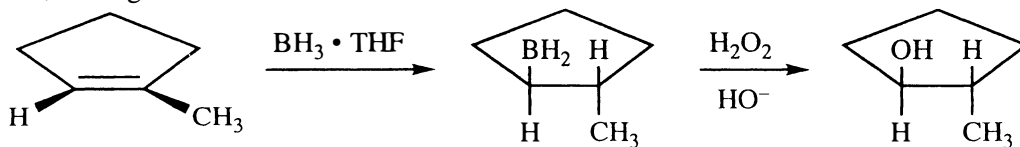
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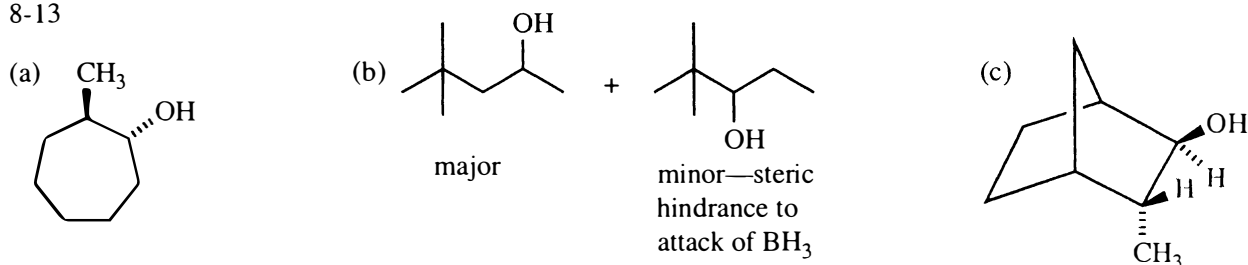
8-11



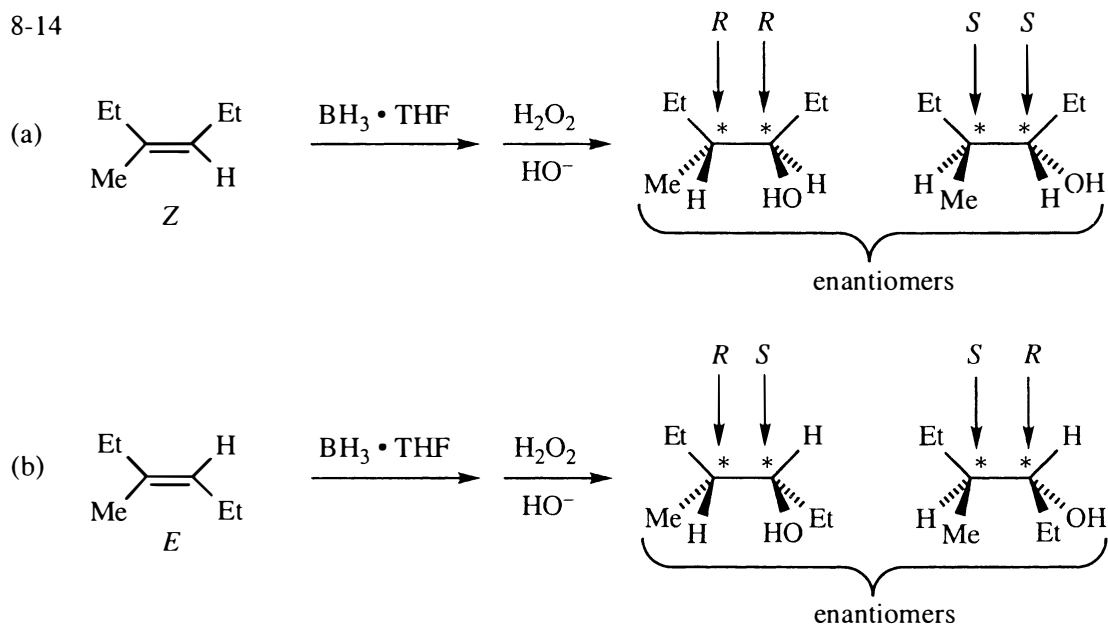
8-12 Instead of borane attacking the bottom face of 1-methylcyclopentene, it is equally likely to attack the top face, leading to the enantiomer.



8-13

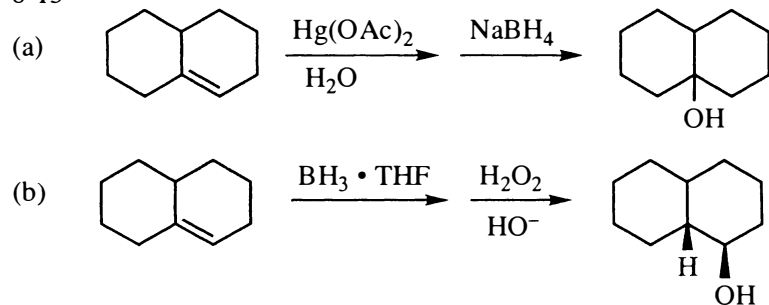


8-14

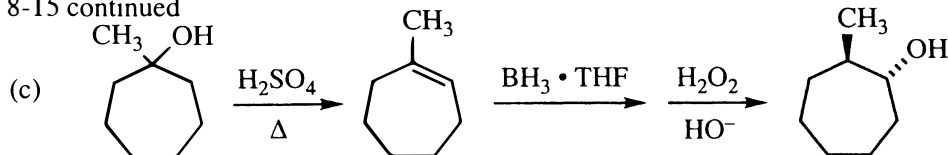


The enantiomeric pair produced from the *Z*-alkene is diastereomeric with the other enantiomeric pair produced from the *E*-alkene. Hydroboration-oxidation is stereospecific, that is, each alkene gives a specific set of stereoisomers, not a random mixture.

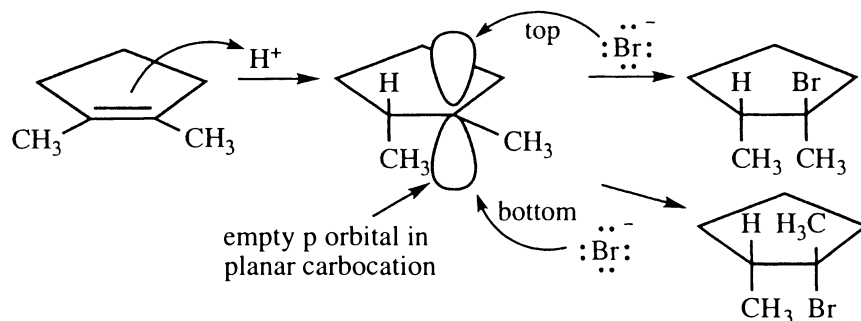
8-15



8-15 continued



8-16

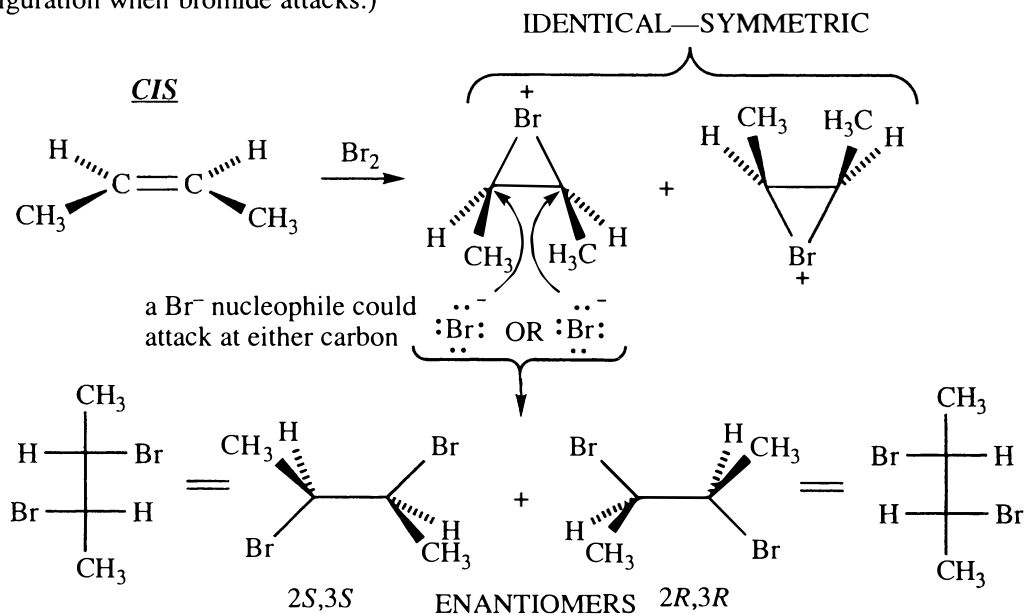


The *planar* carbocation is responsible for non-stereoselectivity. The bromide nucleophile can attack from the top or bottom, leading to a mixture of stereoisomers. The addition is therefore a mixture of syn and anti addition.

8-17 During bromine addition to either the *cis*- or *trans*-alkene, two new chiral centers are being formed. Neither alkene (nor bromine) is optically active, so the product cannot be optically active.

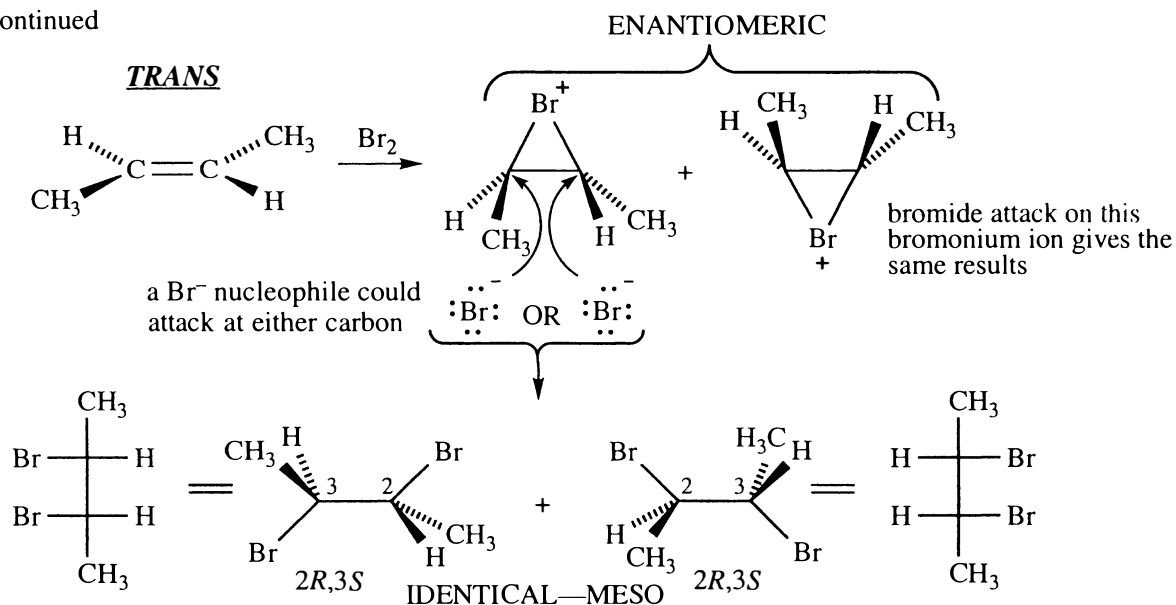
The *cis*-but-2-ene gives two chiral products, a racemic mixture. However, *trans*-but-2-ene, because of its symmetry, gives only one *meso* product which can never be chiral. The "optical *inactivity*" is built into this symmetric molecule.

This can be seen by following what happens to the configuration of the chiral centers from the intermediates to products, below. (The key lies in the symmetry of the intermediate and *inversion* of configuration when bromide attacks.)



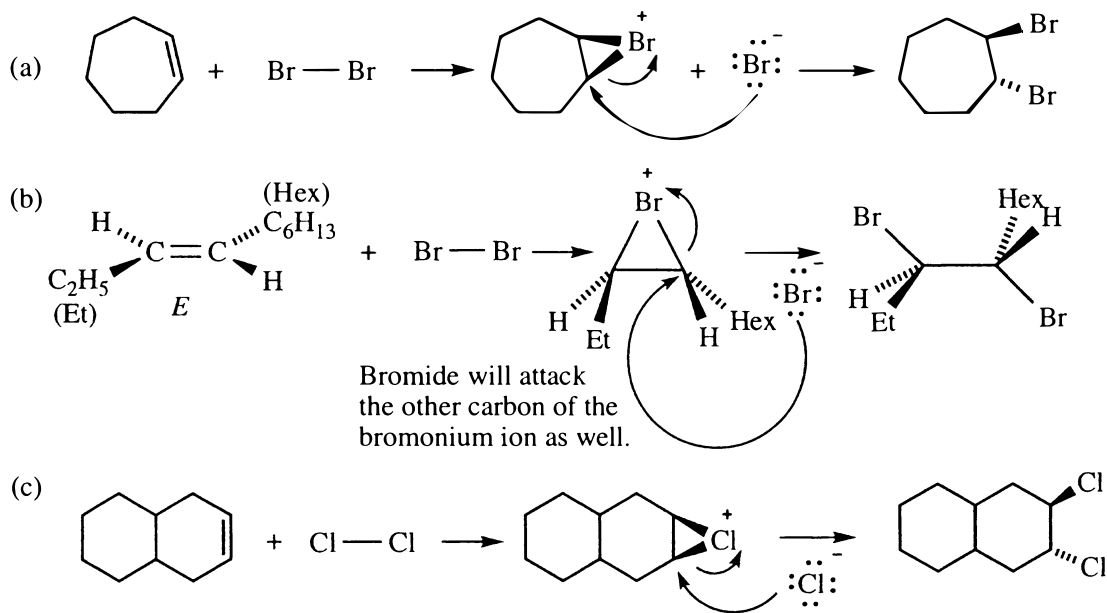
continued on next page

8-17 continued



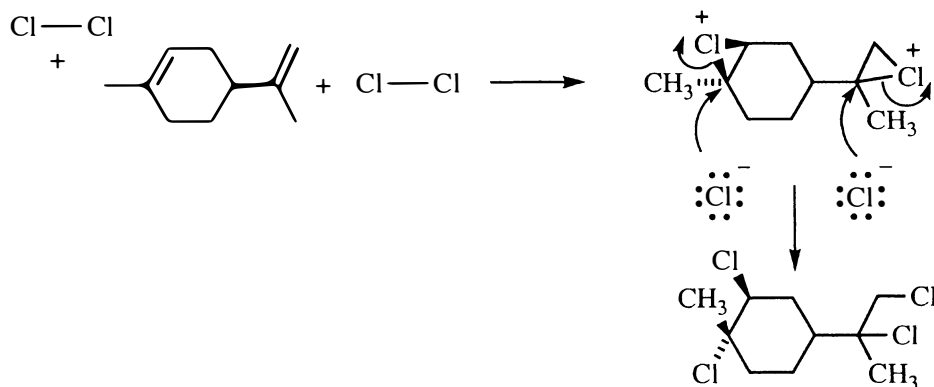
CONCLUSION: anti addition of a symmetric reagent to a symmetric *cis*-alkene gives racemic product, while anti addition to a *trans*-alkene gives meso product. (We will see shortly that syn addition to a *cis*-alkene gives meso product, and syn addition to a *trans*-alkene gives racemic product. Stay tuned.)

8-18 Enantiomers of chiral products are also produced but not shown.

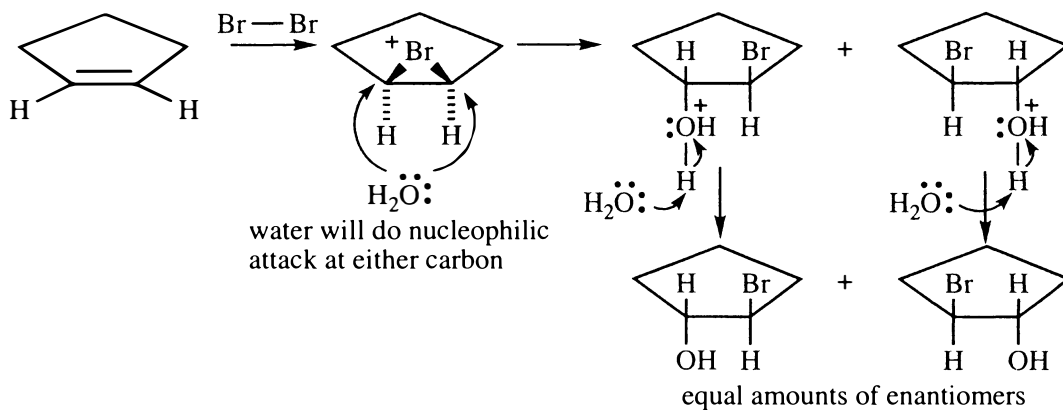


8-18 continued

(d) Three new asymmetric carbons are produced in this reaction. All stereoisomers will be produced with the restriction that the two adjacent chlorines on the ring must be *trans*.



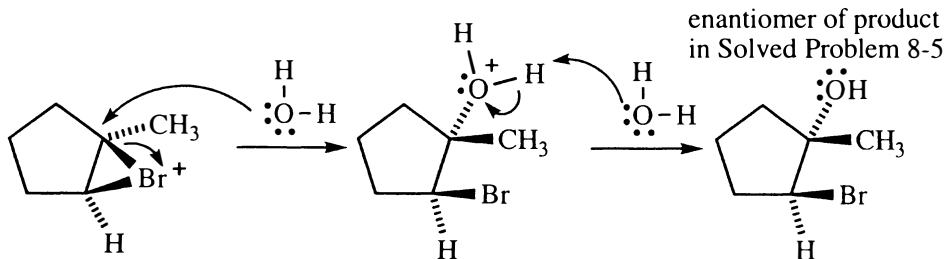
8-19 The *trans* product results from water attacking the bromonium ion from the face opposite the bromine. Equal amounts of the two enantiomers result from the equal probability that water will attack either C-1 or C-2.



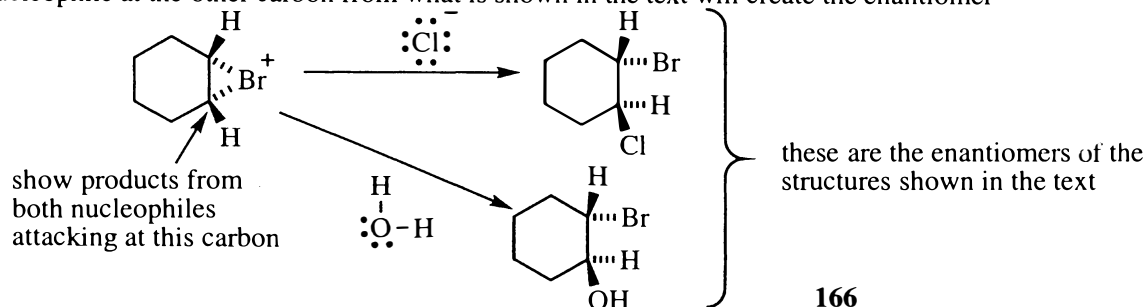
8-20

from Solved Problem 8-5

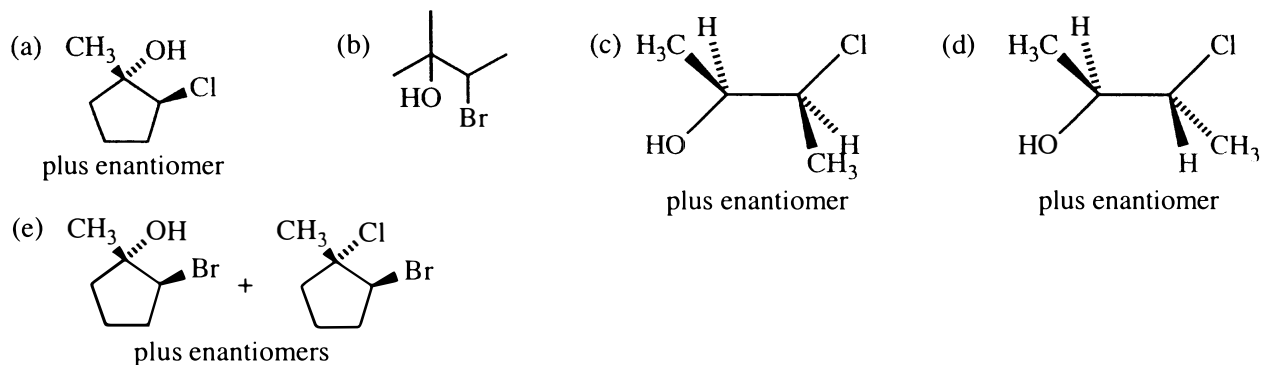
the bromonium ion shown here is the enantiomer of the one shown in Solved Problem 8-5



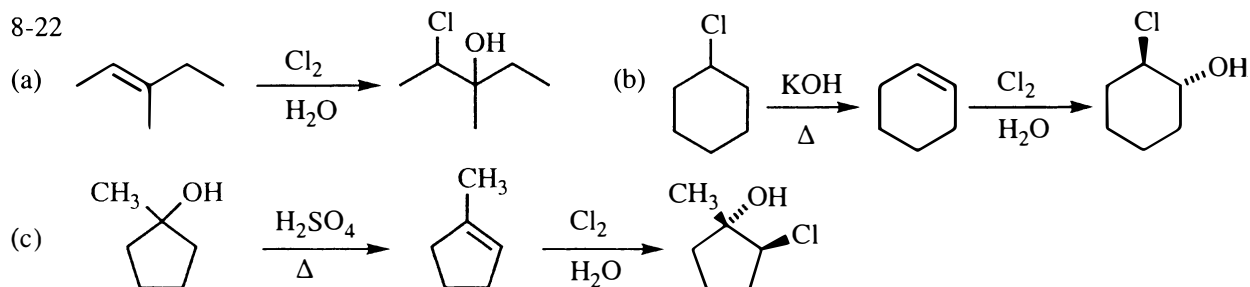
from Solved Problem 8-6: the bromonium ion shown is meso as it has a plane of symmetry; attack by the nucleophile at the other carbon from what is shown in the text will create the enantiomer



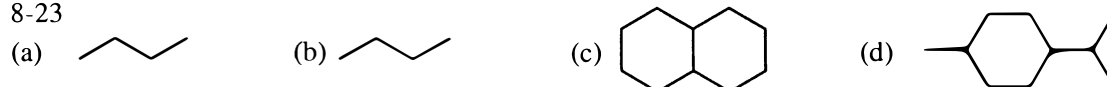
8-21 The chiral products shown here will be racemic mixtures.



8-22

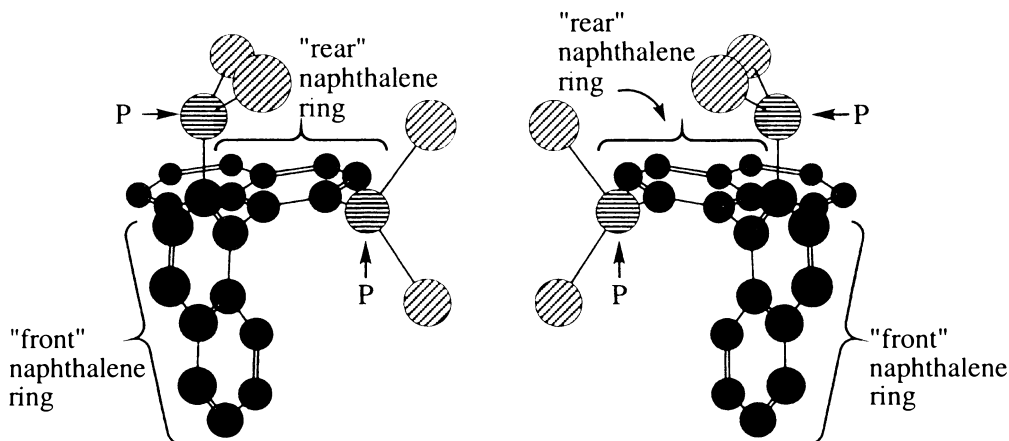


8-23



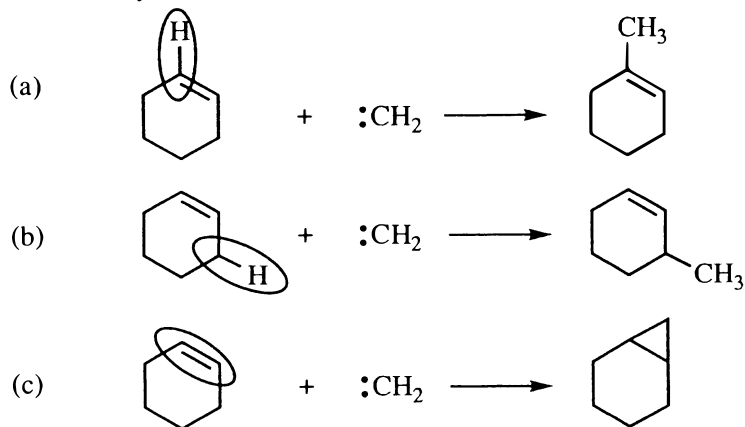
8-24 Limonene, $C_{10}H_{16}$, has three elements of unsaturation. Upon catalytic hydrogenation, the product, $C_{10}H_{20}$, has one element of unsaturation. Two elements of unsaturation have been removed by hydrogenation—these must have been pi bonds, either two double bonds or one triple bond. The one remaining unsaturation must be a ring. Thus, limonene must have one ring and either two double bonds or one triple bond. (The structure of limonene is shown in the text in Problem 8-23(d), and the hydrogenation product is shown above in the solution to 8-23(d).)

8-25 The BINAP ligand is an example of a conformationally hindered biphenyl as described in text section 5-9A and Figure 5-17. The groups are too large to permit rotation around the single bond connecting the rings, so the molecules are locked into one chiral twist or its mirror image.

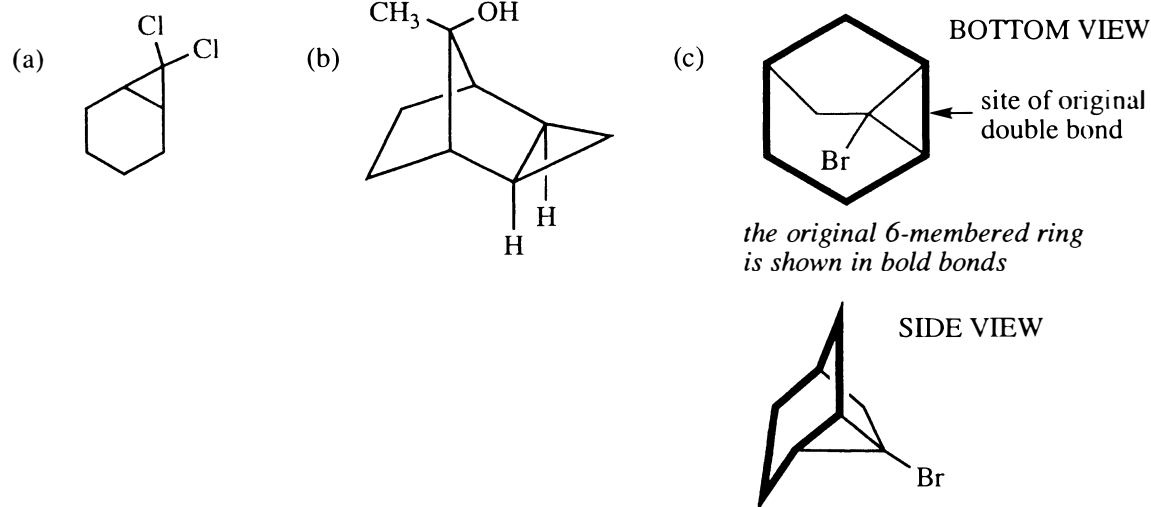


These simplified three-dimensional drawings of the enantiomers show that the two naphthalene rings are twisted almost perpendicular to each other, and the large $-P(Ph)_2$ substituents prevent interconversion of these mirror images.

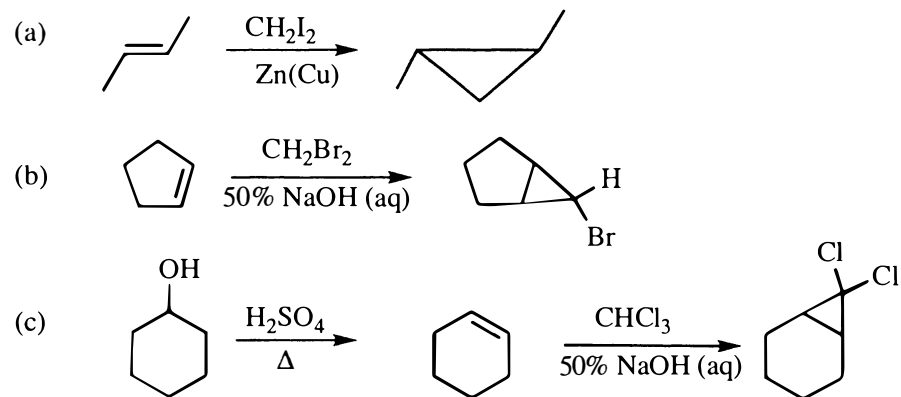
8-26 Methylene inserts into the circled bonds.



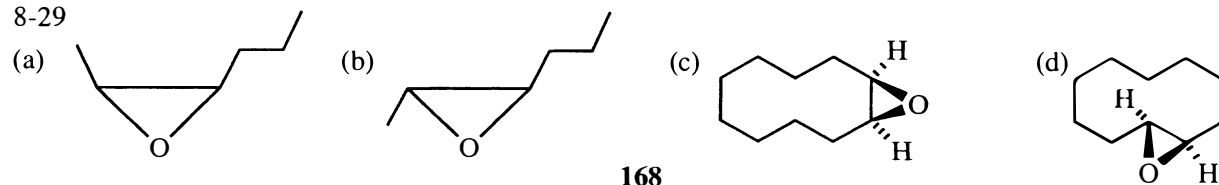
8-27



8-28

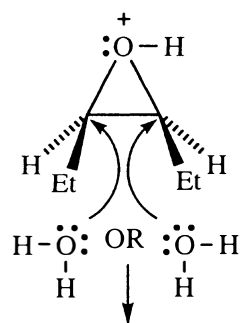
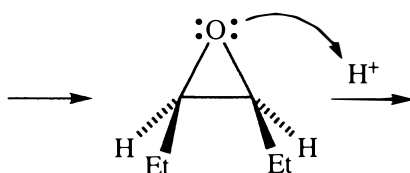
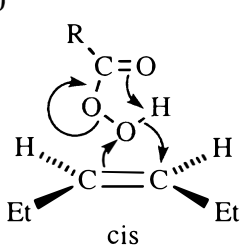


8-29

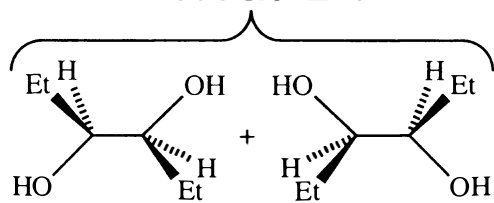
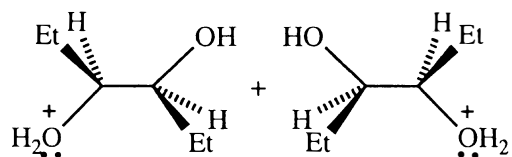


8-30

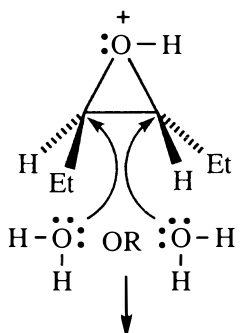
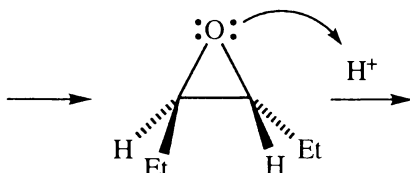
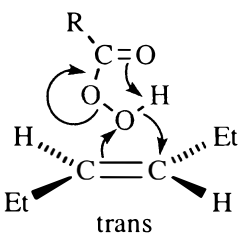
(a)



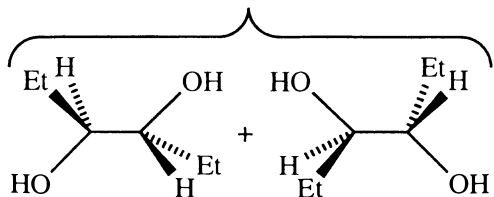
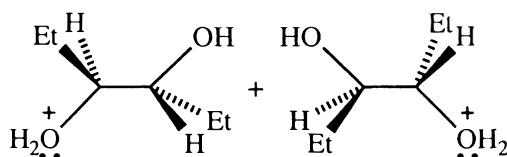
ENANTIOMERS

 $-H^+$ 

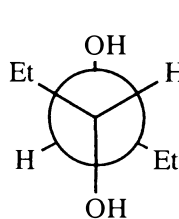
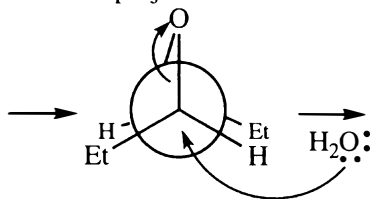
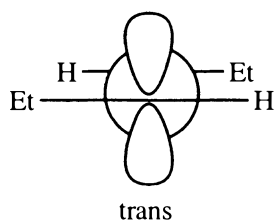
(b)



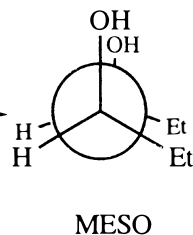
IDENTICAL—MESO

 $-H^+$ 

stereochemistry shown in Newman projections:

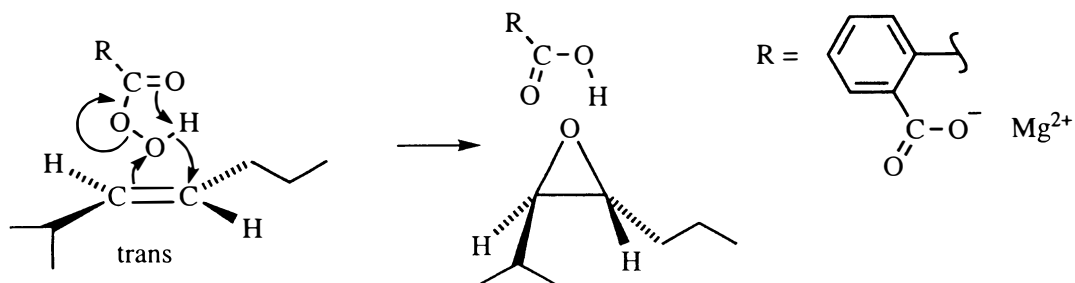


rotate

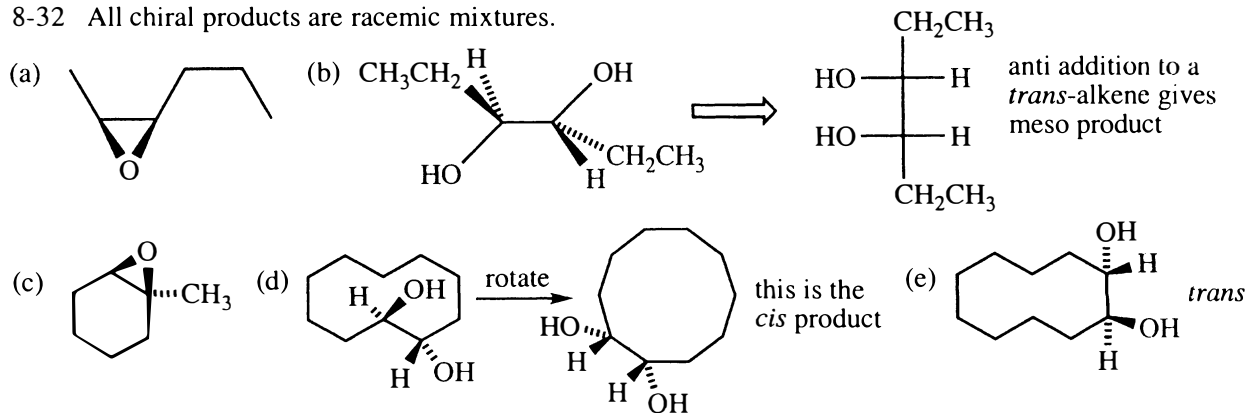


Remember the lesson from Problem 8-17: anti addition of a symmetric reagent to a symmetric *cis*-alkene gives racemic product, while anti addition to a *trans*-alkene gives meso product. This fits the definition of a *stereospecific* reaction, where different stereoisomers of the starting material (*cis* and *trans*) are converted into different stereoisomers of product (a *dl*-pair and *meso* form).

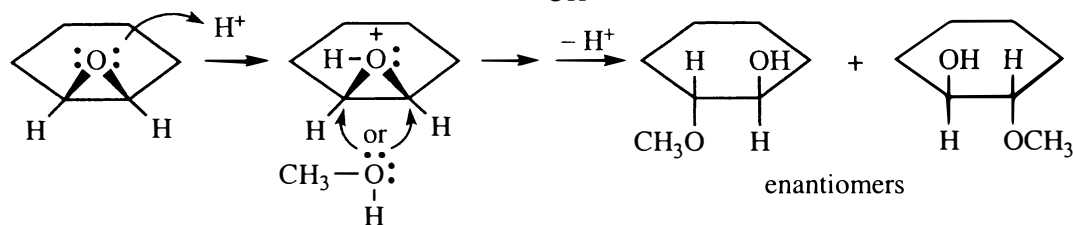
8-31



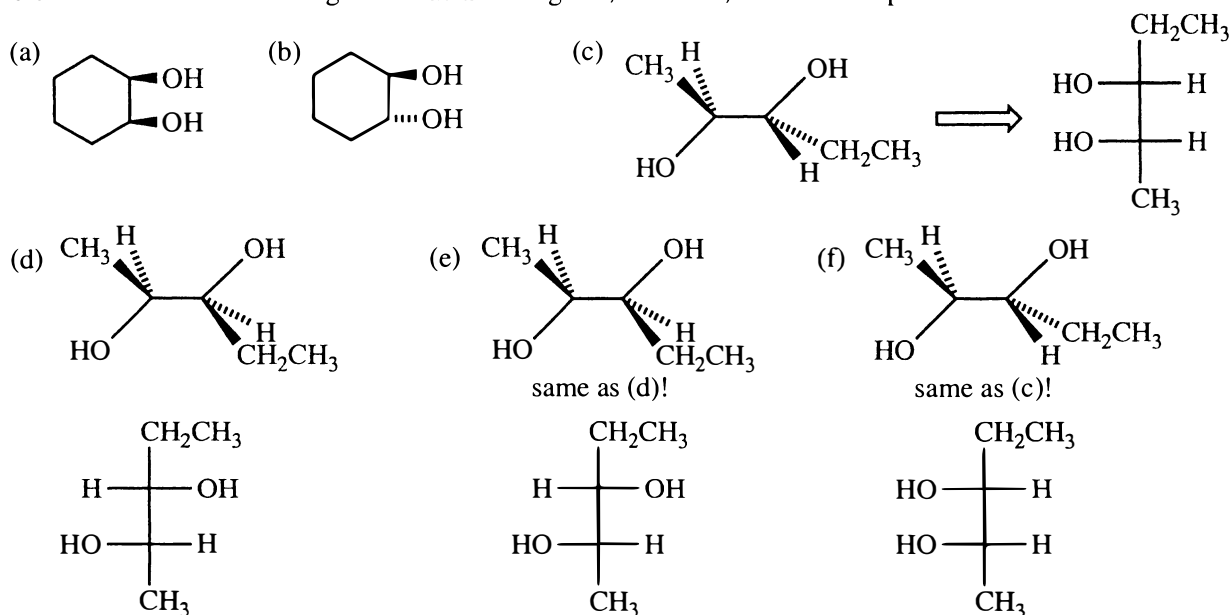
8-32 All chiral products are racemic mixtures.



8-33

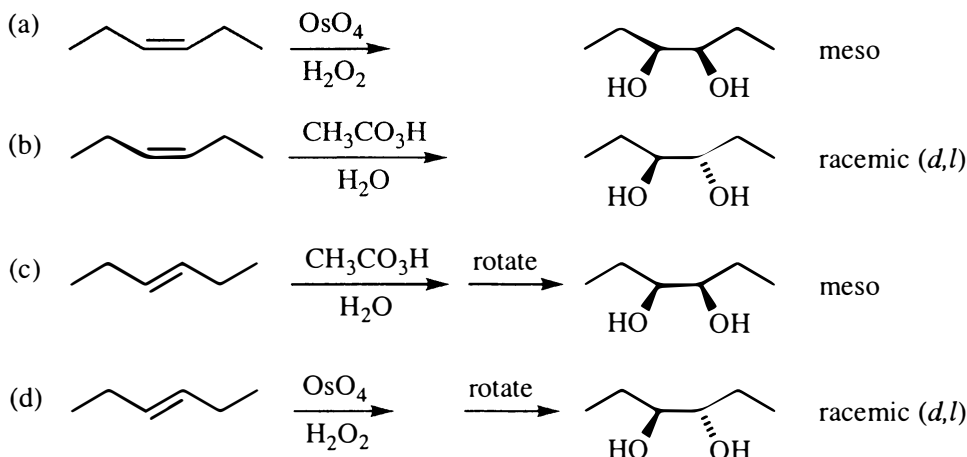


8-34 All these reactions begin with achiral reagents; therefore, all the chiral products are racemic.



Refer to the observation in the solution to Problem 8-35 on the next page.

8-35



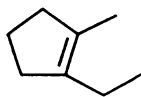
Have you noticed yet? For symmetric alkenes and symmetric reagents (addition of two identical X groups):

cis-alkene + **syn** addition → meso
cis-alkene + **anti** addition → racemic
trans-alkene + **syn** addition → racemic
trans-alkene + **anti** addition → meso

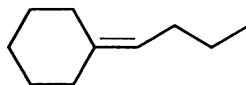
Assume that <i>cis</i> / <i>syn</i> / <i>meso</i>	+1 x +1 = +1
are "same", and <i>trans</i> / <i>anti</i> / <i>racemic</i>	+1 x -1 = -1
are "opposite".	
Then any combination can	-1 x +1 = -1
be predicted, just like math!	-1 x -1 = +1

8-36 Solve these ozonolysis problems by working backwards, that is, by "reattaching" the two carbons of the new carbonyl groups into alkenes. Here's a hint. When you cut a circular piece of string, you still have only one piece. When you cut a linear piece of string, you have two pieces. Same with molecules. If ozonolysis forms only one product with two carbonyls, the alkene had to have been in a ring. If ozonolysis gives two molecules, the alkene had to have been in a chain.

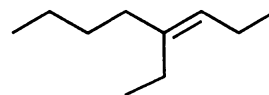
(a) two carbonyls from ozonolysis are in a chain, so alkene had to have been in a ring



(b) two carbonyls from ozonolysis are in two different products, so alkene had to have been in a chain, not a ring

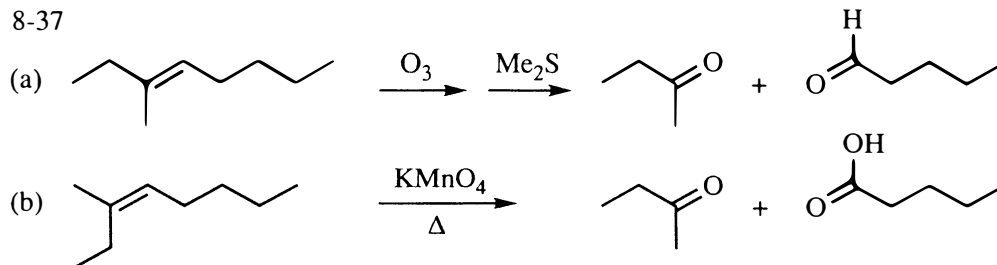


(c) two carbonyls from ozonolysis are in two different products, so alkene had to have been in a chain, not a ring

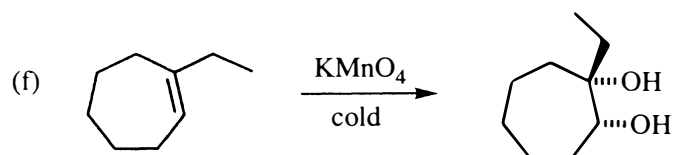
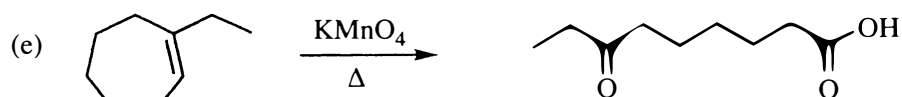
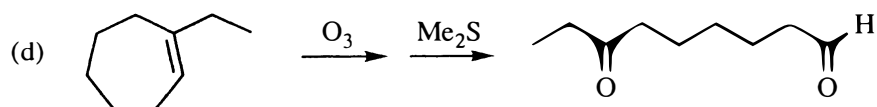
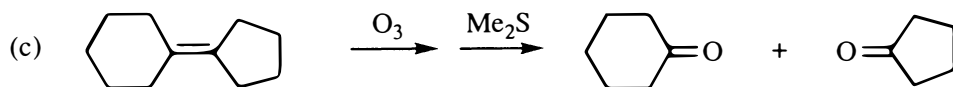


E or *Z* of alkene cannot be determined from products

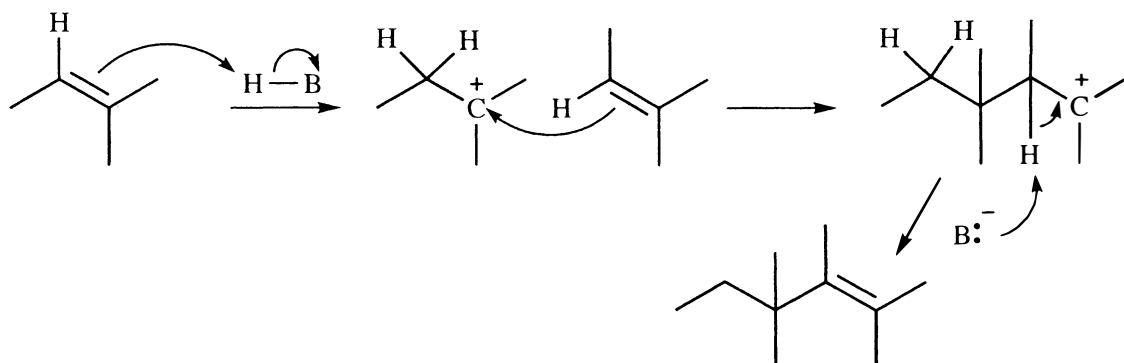
8-37



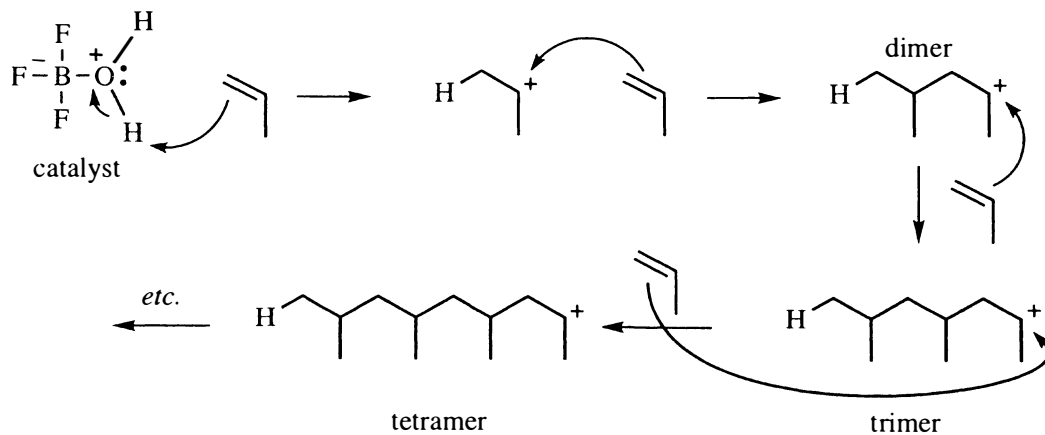
8-37 continued



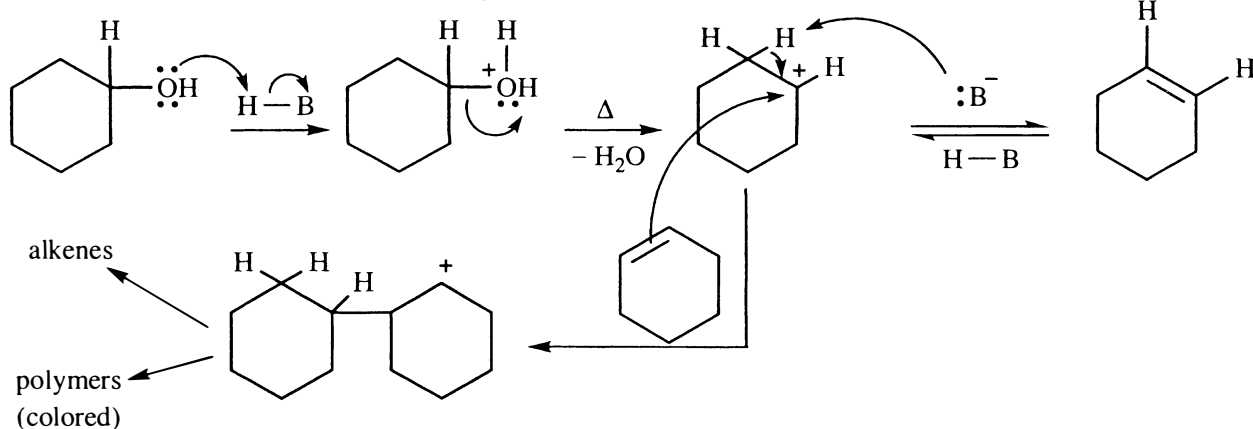
8-38 The representation for a generic acid will be $\text{H}-\text{B}$, where B is the conjugate base.



8-39 Catalytic BF_3 reacts with trace amounts of water to form the probable catalyst:

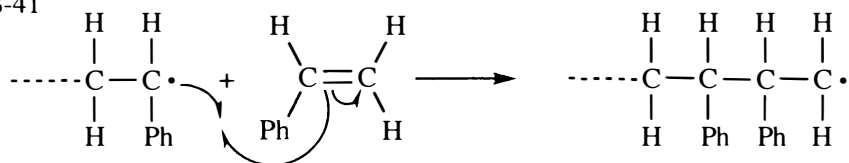


8-40 H—B is used here to symbolize a generic acid.



Note: the dashed bond symbol is used here to indicate the continuation of a polymer chain.

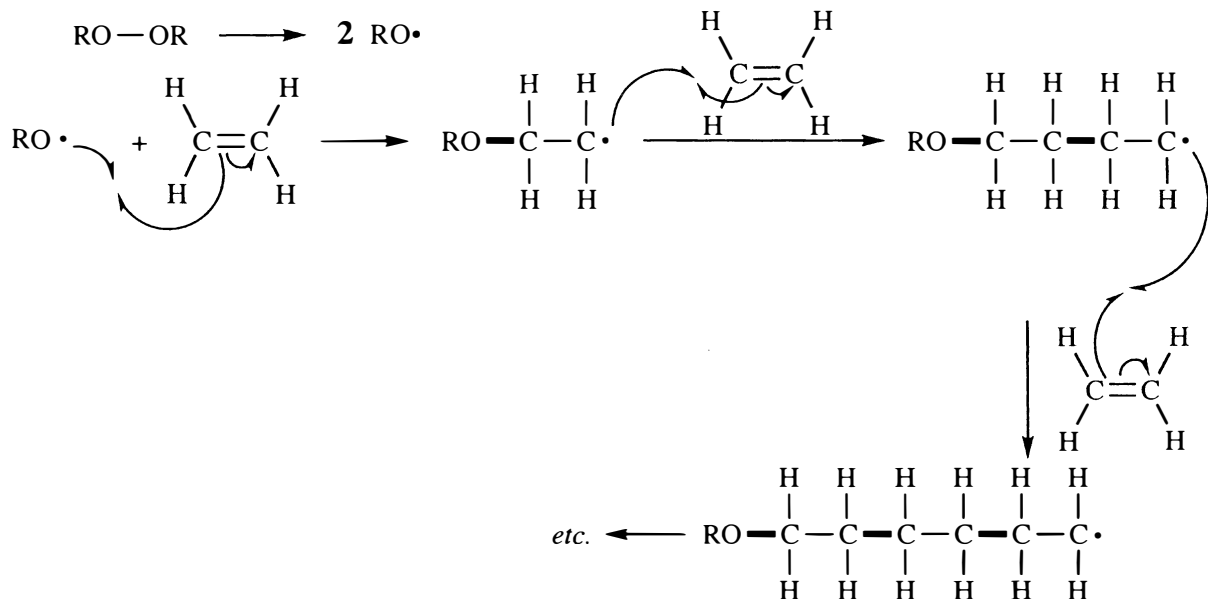
8-41



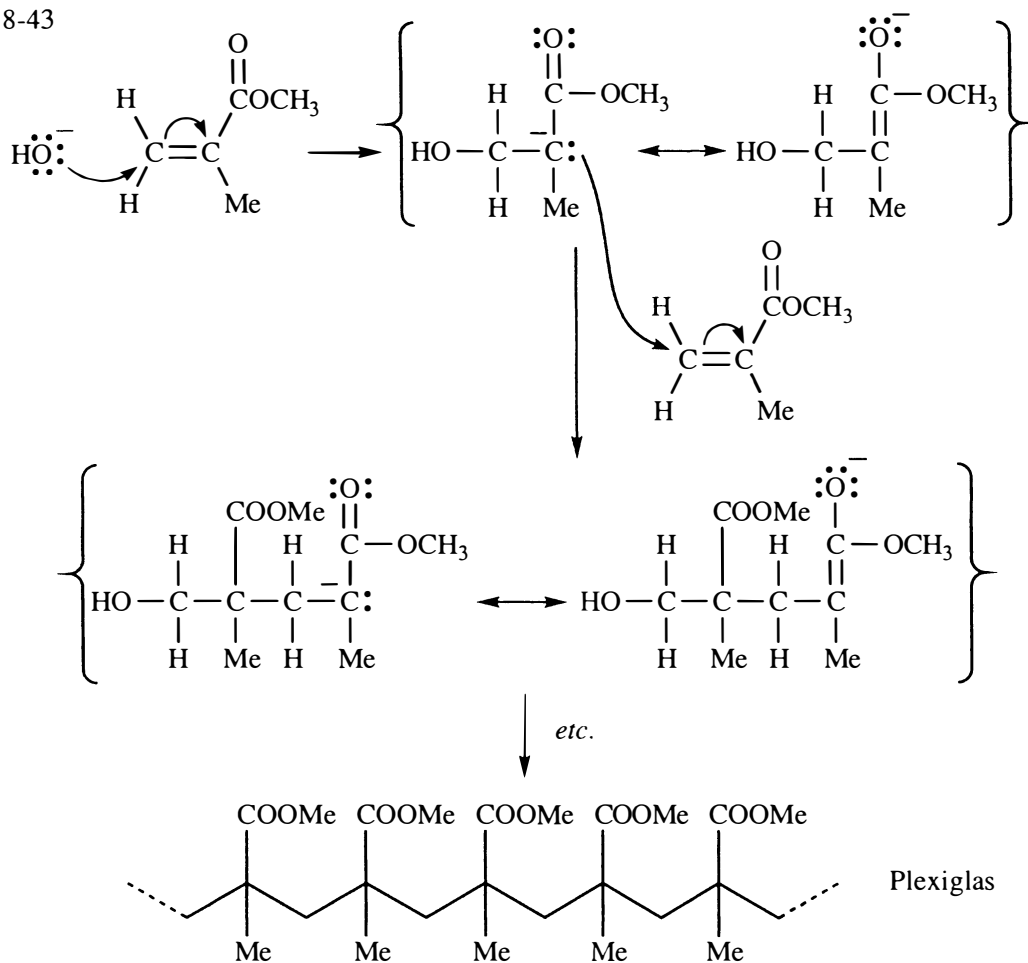
1° radical, and *not* resonance-stabilized—
this orientation is not observed

Orientation of addition always generates the more stable intermediate; the energy difference between a 1° radical (shown above) and a benzylic radical is huge. The phenyl substituents must necessarily be on alternating carbons because the orientation of attack is always the same—not a random process.

8-42 For clarity, the new bonds formed in this mechanism are shown in bold.

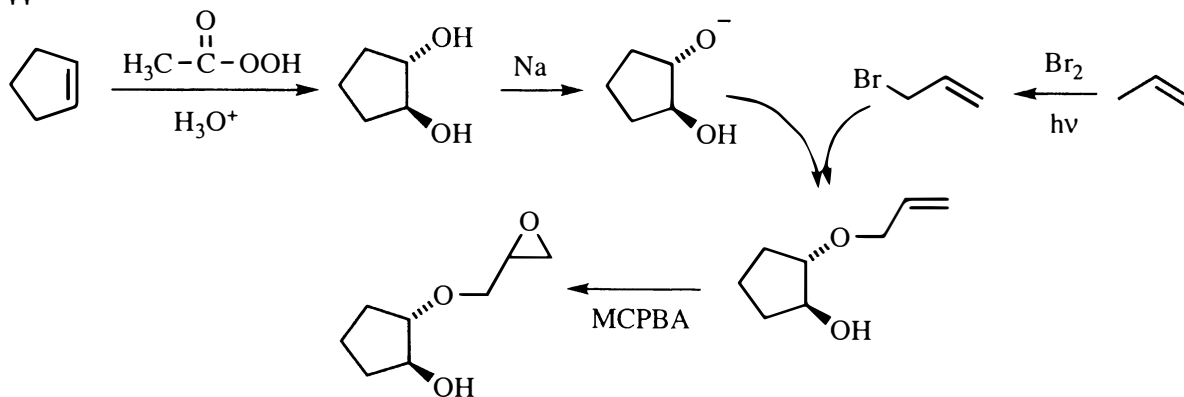


8-43

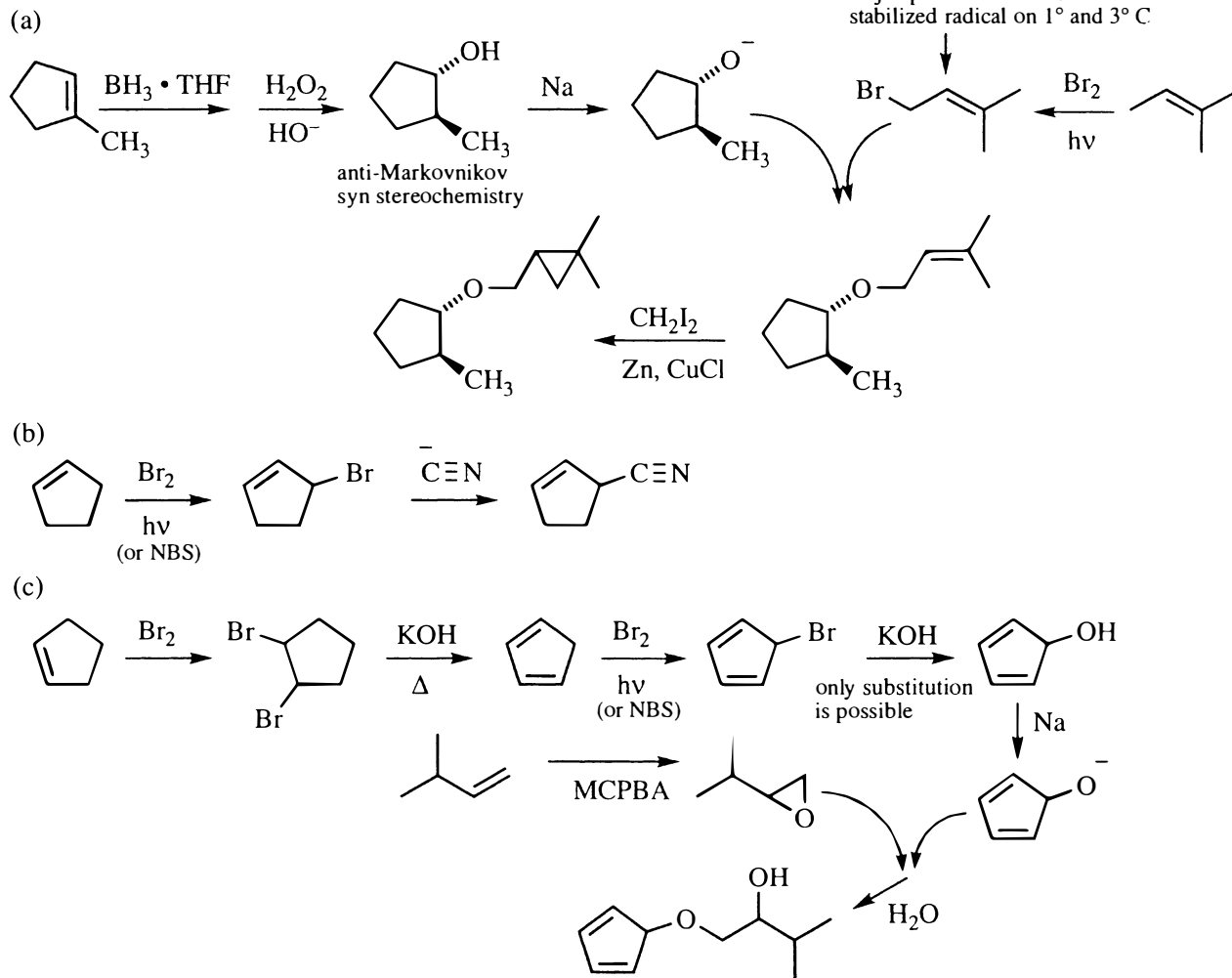


Dashed bonds mean that the chain continues.

8-44

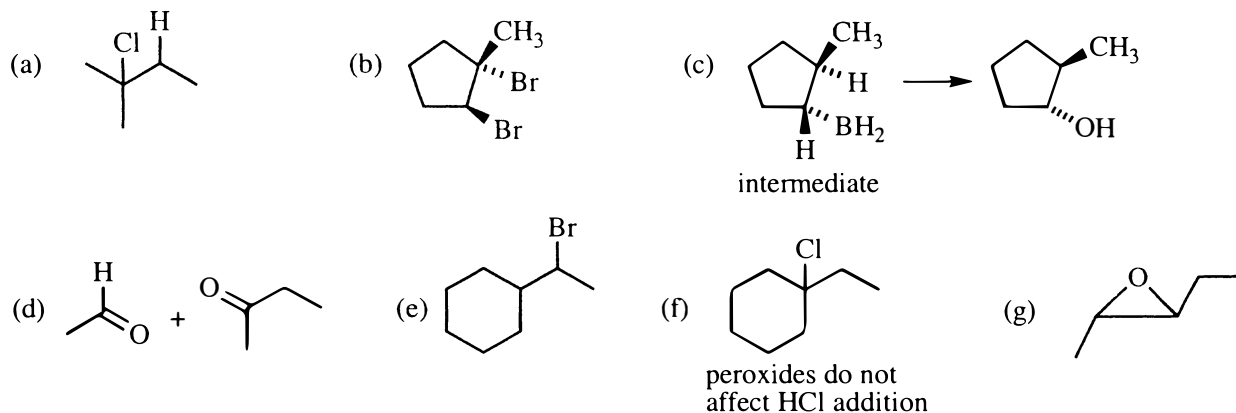


8-45 In the spirit of this problem, all starting materials will have six carbons or fewer and only one carbon-carbon double bond. Reagents may have other atoms.

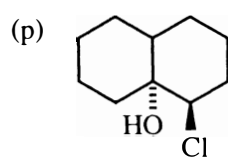
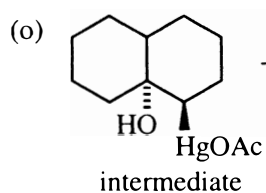
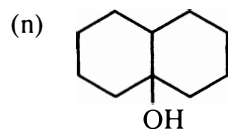
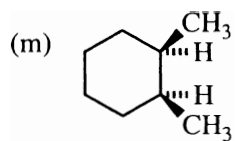
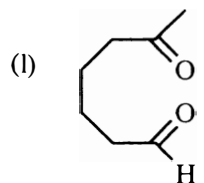
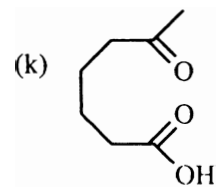
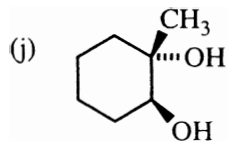
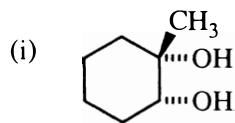
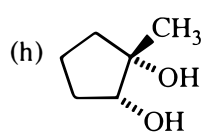


8-46 Please refer to solution 1-20, page 12 of this Solutions Manual.

8-47



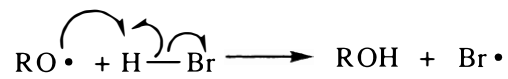
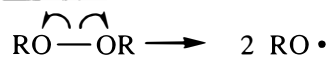
8-47 continued



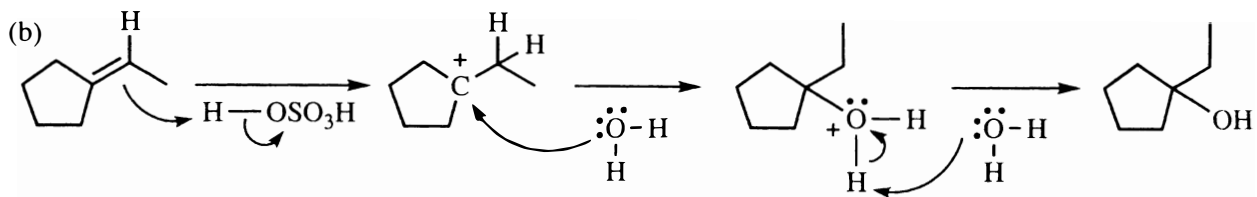
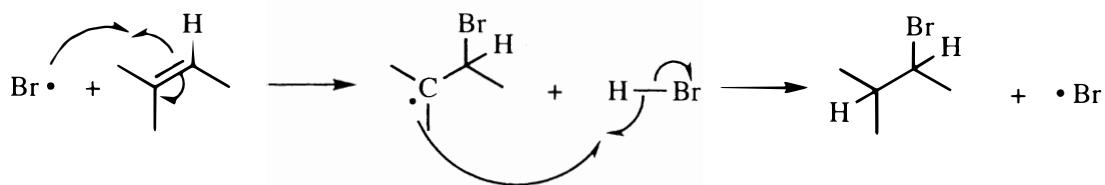
8-48

(a)

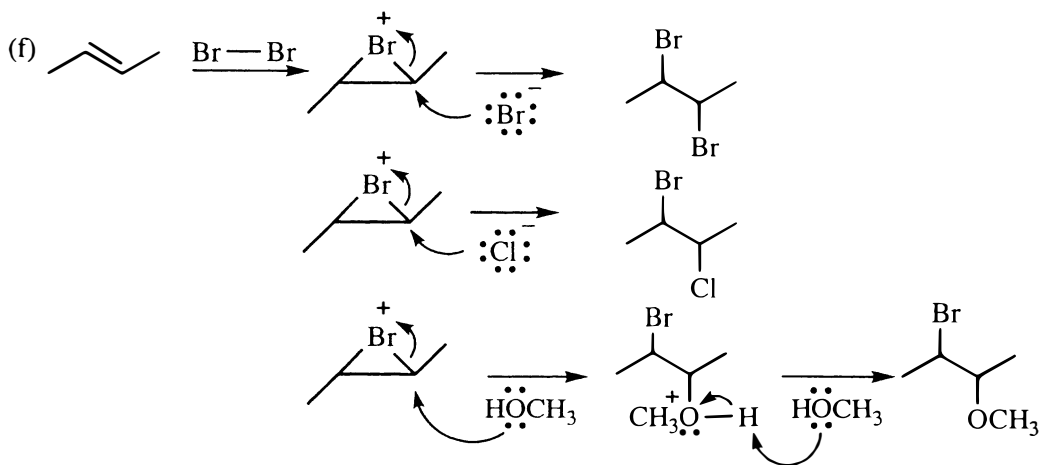
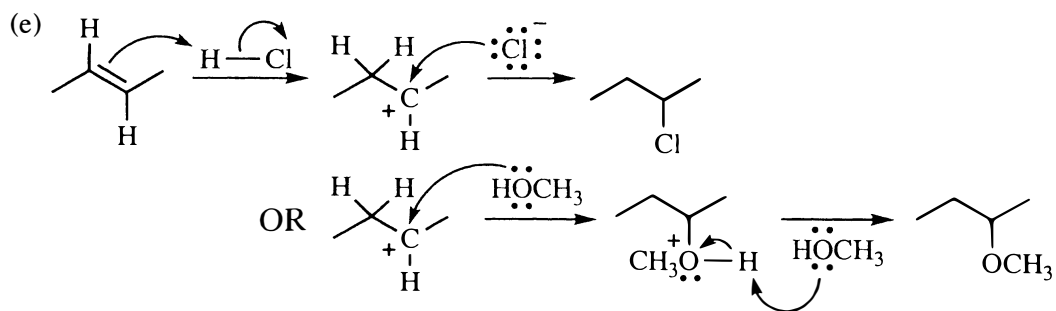
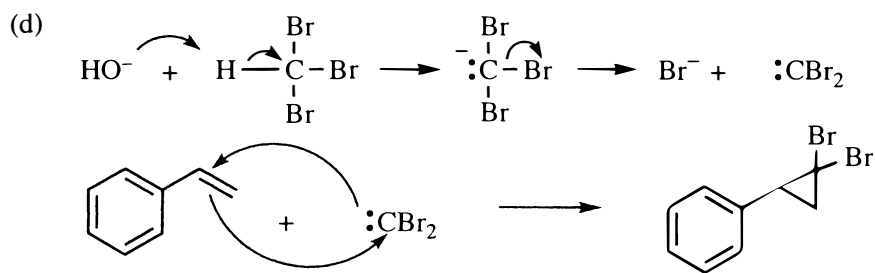
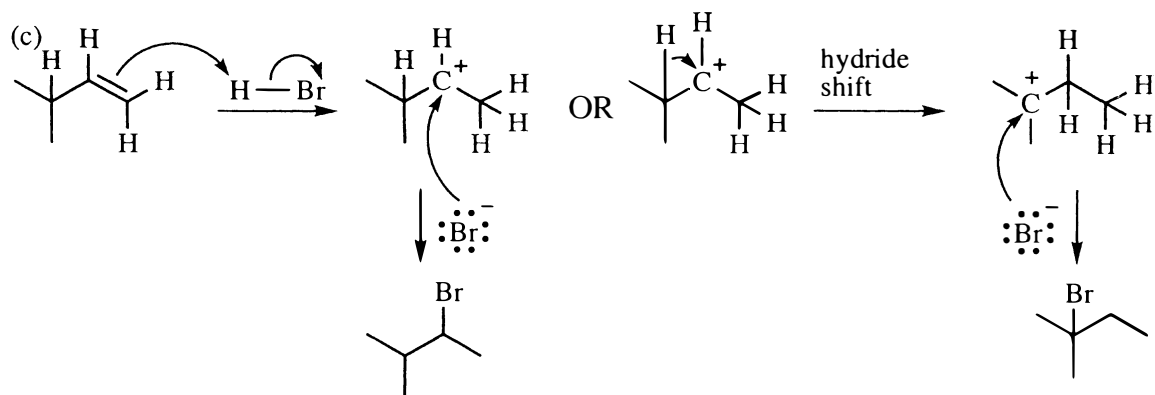
initiation



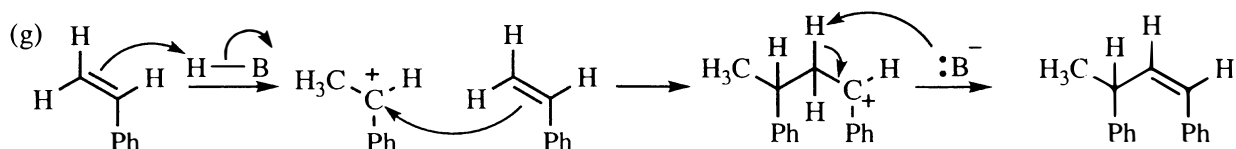
propagation



8-48 continued

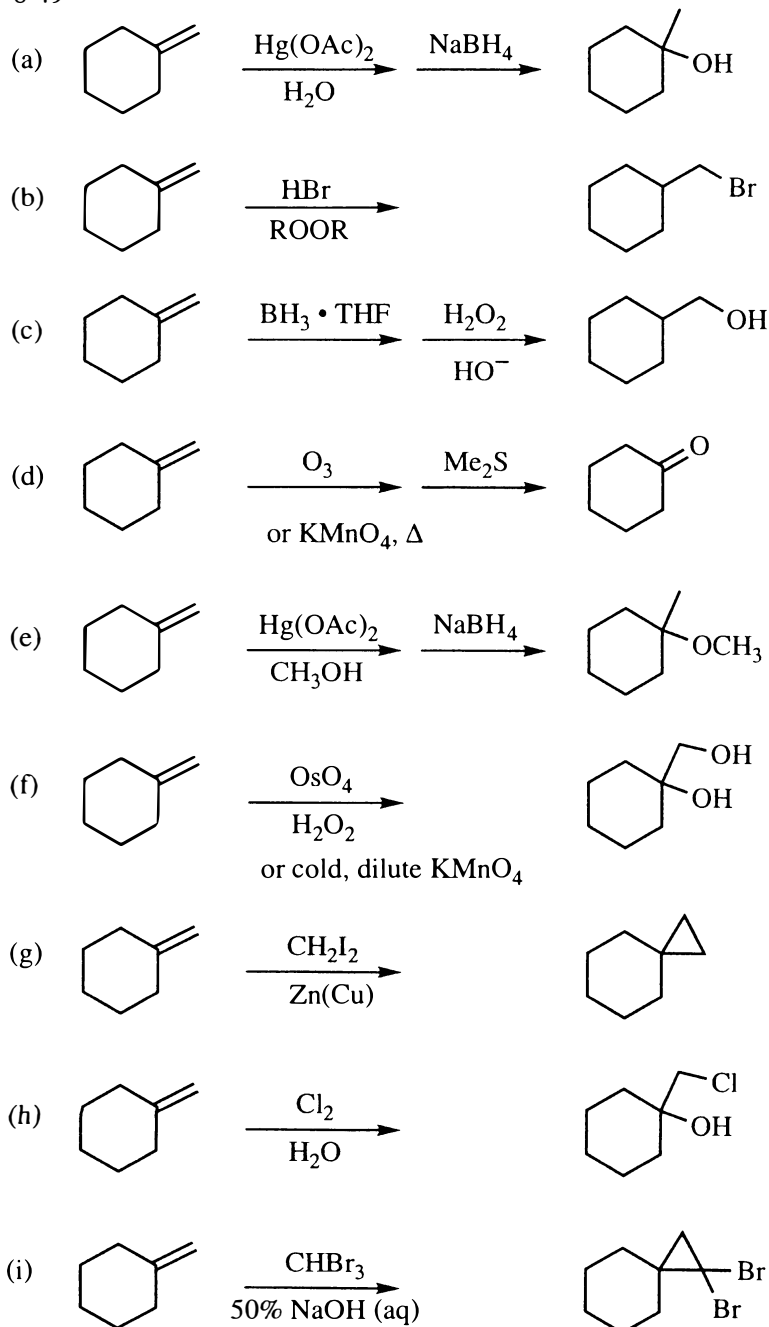


8-48 continued

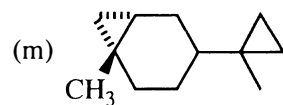
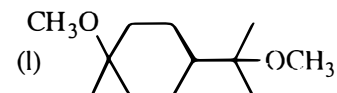
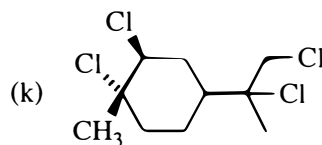
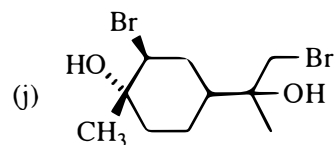
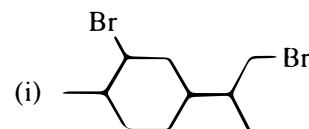
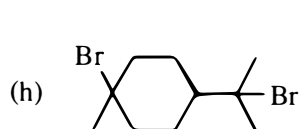
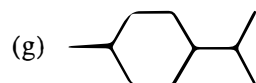
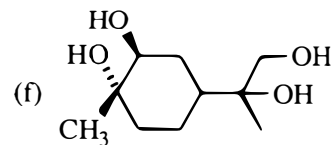
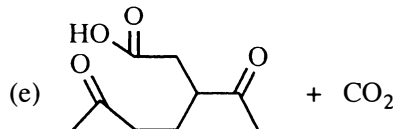
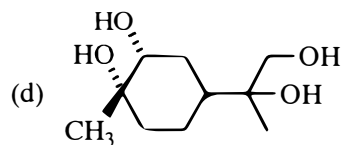
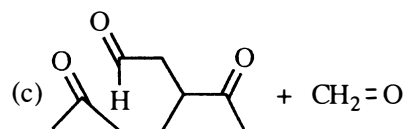
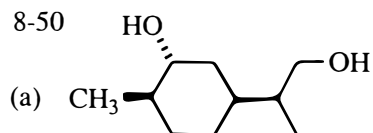


Recall that "Ph" is the abbreviation for phenyl.

8-49

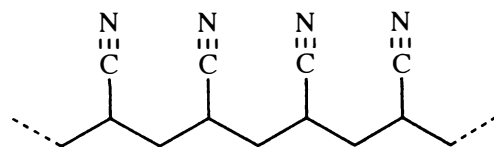
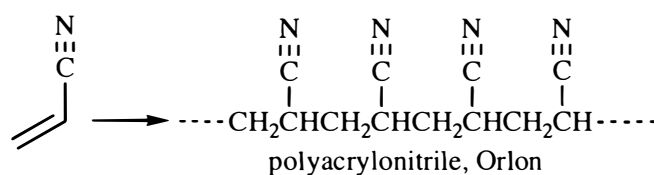
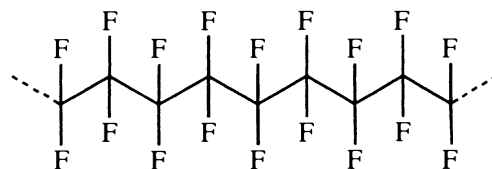
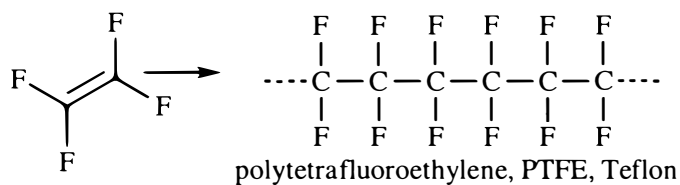
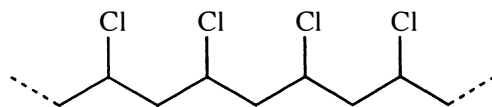
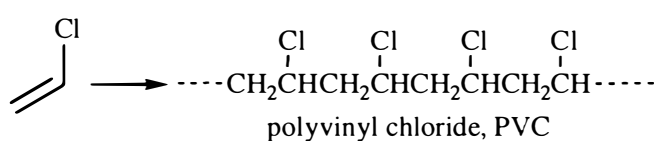


8-50

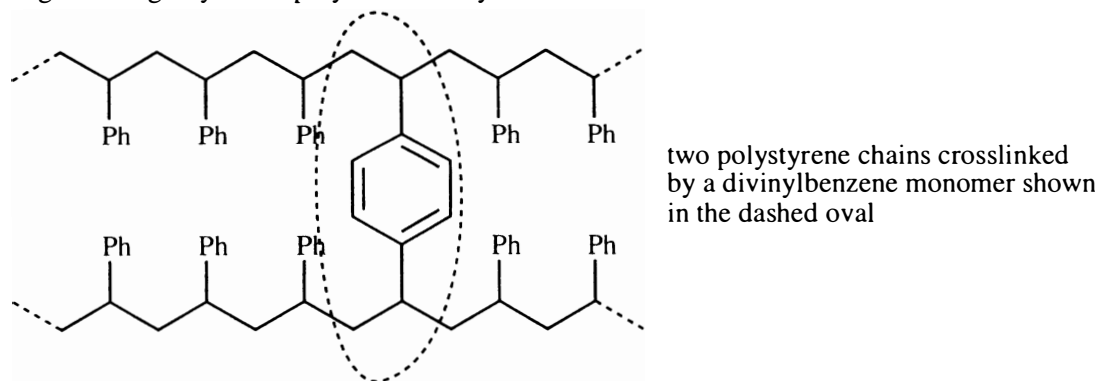


8-51 Each monomer has two carbons in the backbone, so the substituents on the monomer will repeat every two carbons in the polymer. Dashed bonds indicate continuation of the polymer chain.

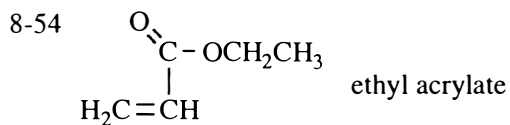
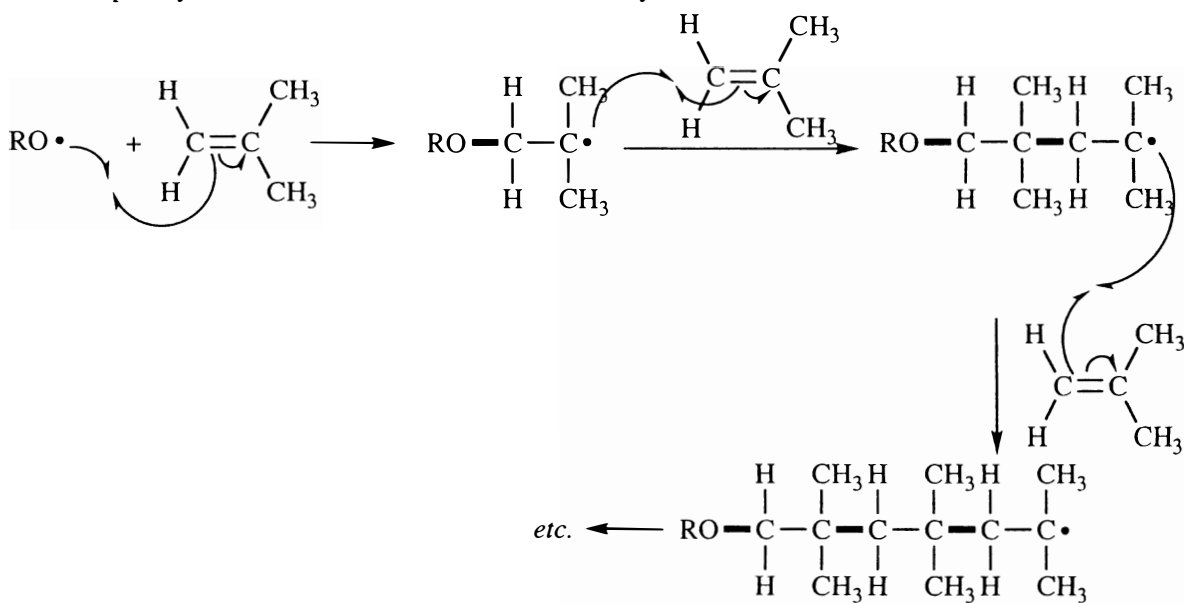
line formula representation



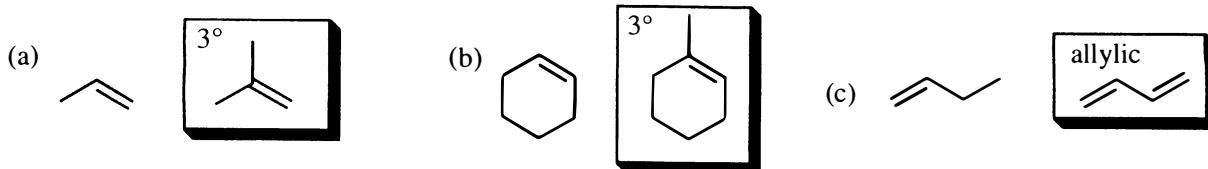
8-52 Without divinylbenzene, individual chains of polystyrene are able to slide past one another. Addition of divinylbenzene during polymerization forms bridges, or "crosslinks", between chains, adding strength and rigidity to the polymer. Divinylbenzene and similar molecules are called crosslinking agents.



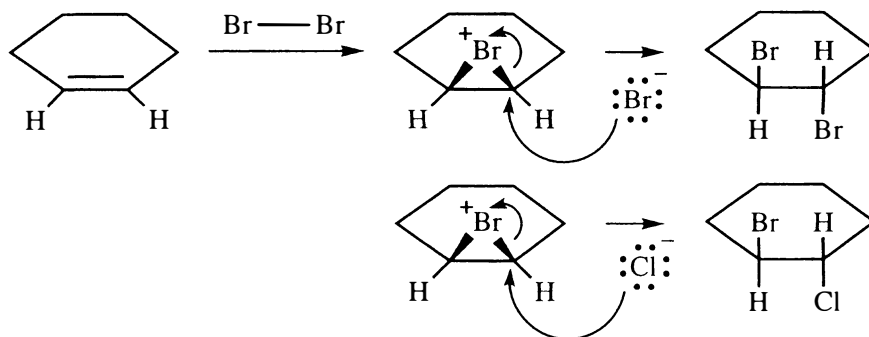
8-53 A peroxy radical is shown as the initiator. Newly formed bonds are shown in bold.



8-55 In each case, the compound (boxed) that produces the more stable carbocation is more reactive.

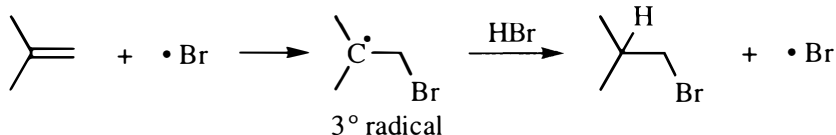


8-56 Once the bromonium ion is formed, it can be attacked by either nucleophile, bromide or chloride, leading to the mixture of products.

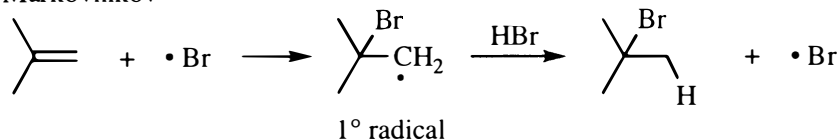


8-57 Two possible orientations of attack of bromine radical are possible:

(A) anti-Markovnikov



(B) Markovnikov



The first step in the mechanism is endothermic and rate determining. The 3° radical produced in anti-Markovnikov attack (A) of bromine radical is several kJ/mole more stable than the 1° radical generated by Markovnikov attack (B). The Hammond Postulate tells us that it is reasonable to assume that the activation energy for anti-Markovnikov addition is lower than for Markovnikov addition. This defines the first half of the energy diagram.

The relative stabilities of the final products are somewhat difficult to predict. (Remember that stability of final products does not necessarily reflect relative stabilities of intermediates; this is why a thermodynamic product can be different from a kinetic product.) From bond dissociation energies (kJ/mole) in Table 4-2:

anti-Markovnikov

H to 3° C 381

Br to 1° C 285
666 kJ/mole

Markovnikov

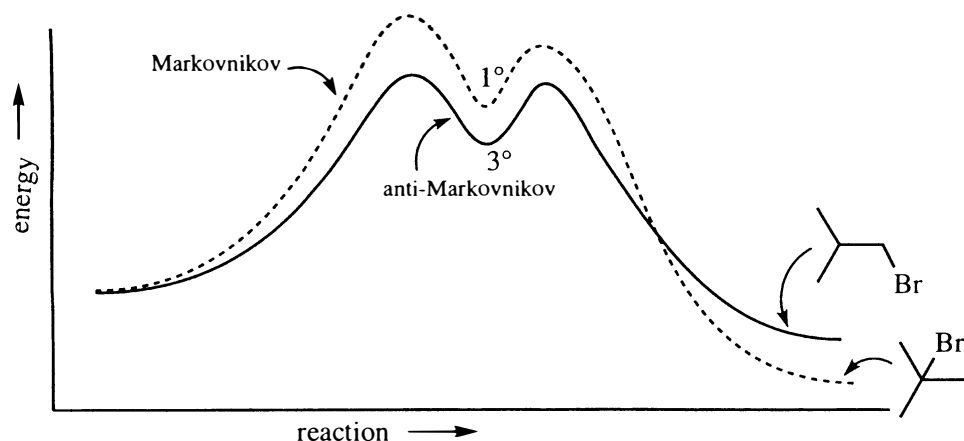
H to 1° C 410

Br to 3° C 272
682 kJ/mole

If it takes more energy to break bonds in the Markovnikov product, it must be lower in energy, therefore, more stable—OPPOSITE OF STABILITY OF THE INTERMEDIATES!

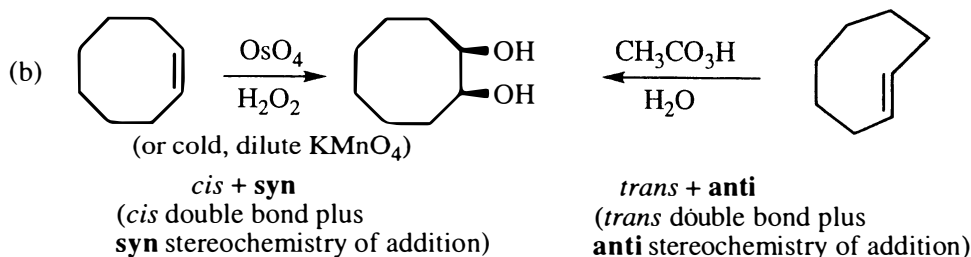
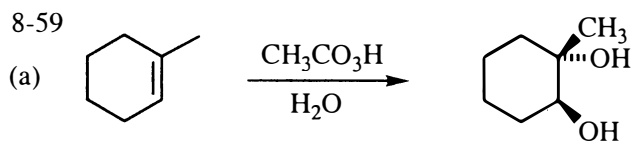
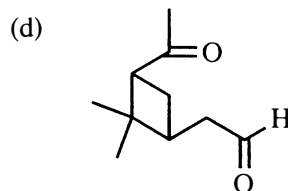
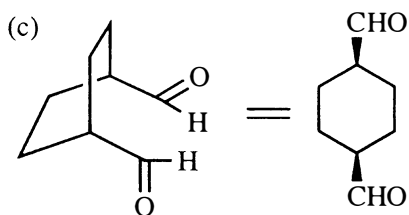
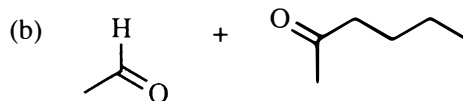
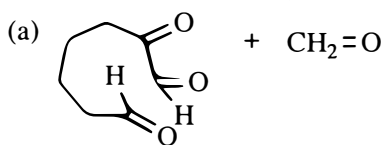
Now we are ready to construct the energy diagram; see the next page.

8-57 continued

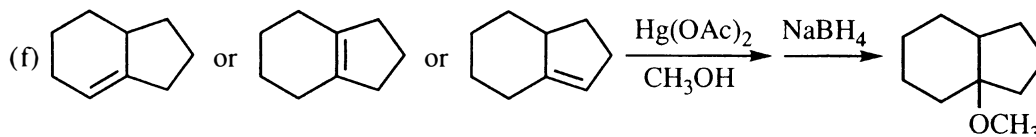
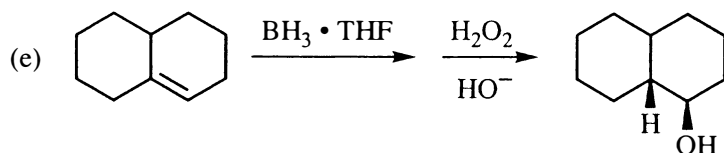
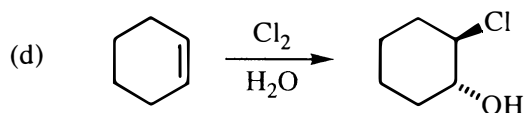
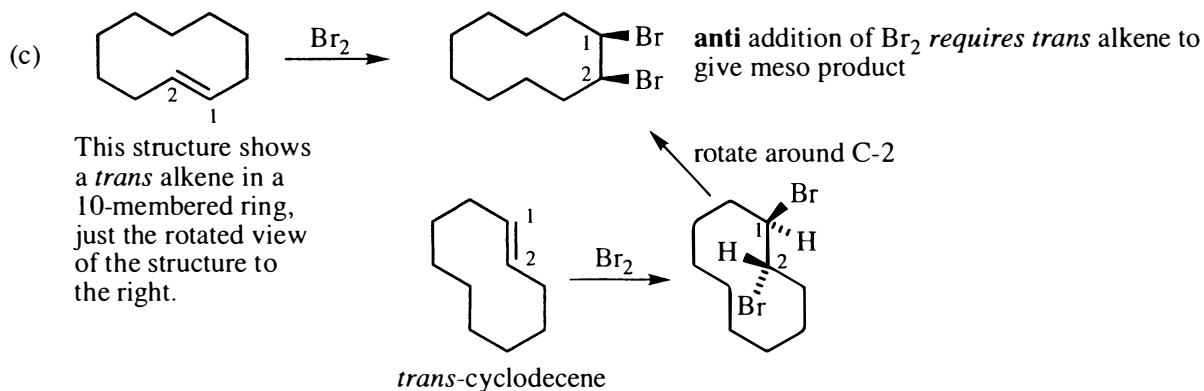


It is the anti-Markovnikov product that is the kinetic product, not the thermodynamic product; the anti-Markovnikov product is obtained since its rate-determining step has the lower activation energy.

8-58 Recall these facts about ozonolysis: each alkene cleaved by ozone produces two carbonyl groups; an alkene in a chain produces two separate products; an alkene in a ring produces one product in which the two carbonyls are connected.



8-59 continued



8-60

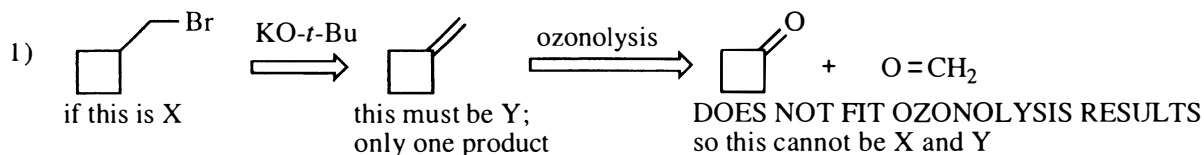
A) Unknown X, C₅H₉Br, has one element of unsaturation. X reacts with neither bromine nor KMnO₄, so the unsaturation in X cannot be an alkene; it must be a ring.

B) Upon treatment with strong base (*t*-butoxide), X loses H and Br to give Y, C₅H₈, which does react with bromine and KMnO₄; it must have an alkene and a ring. Only one isomer is formed.

C) Catalytic hydrogenation of Y gives methylcyclobutane. This is a BIG clue because it gives the carbon skeleton of the unknown. Y must have a double bond in the methylcyclobutane skeleton, and X must have a Br on the methylcyclobutane skeleton.

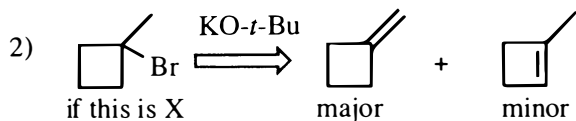
D) Ozonolysis of Y gives a dialdehyde Z, C₅H₈O₂, which contains all the original carbons, so the alkene cleaved in the ozonolysis had to be in the ring.

Let's consider the possible answers for X and see if each fits the information.

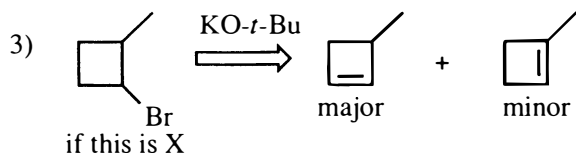


more possibilities on the next page

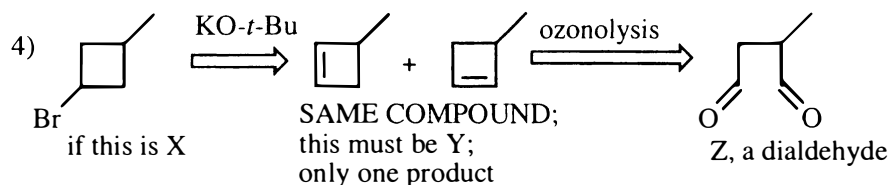
8-60 continued



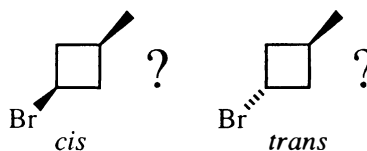
Y would be a mixture of alkenes, but the elimination gives only one product. We already saw in example 1 that the exocyclic double bond does not fit the ozonolysis results so this structure cannot be X.



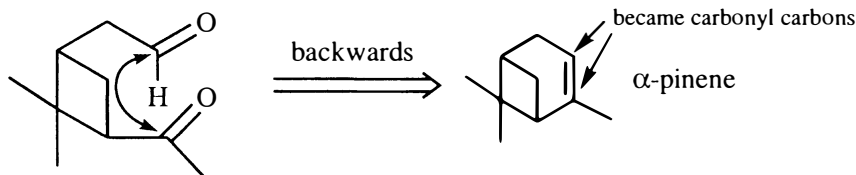
Y would be a mixture of alkenes, but the elimination gives only one product, so this structure of X is not consistent with the information provided.



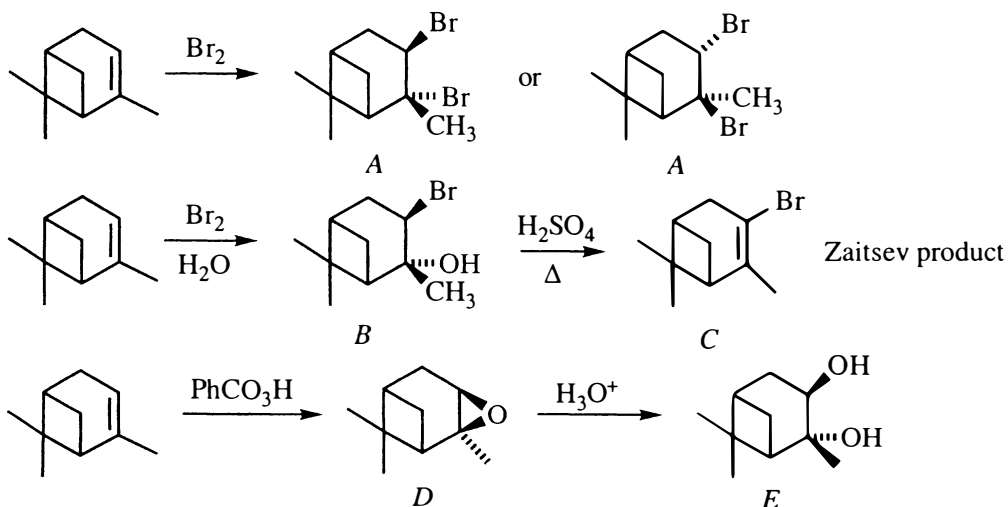
The correct structures for X, Y, and Z are given in the fourth possibility. The only structural feature of X that remains undetermined is whether it is the *cis* or *trans* isomer.



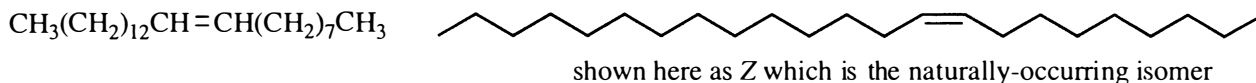
8-61 The clue to the structure of α -pinene is the ozonolysis. Working backwards shows the alkene position.



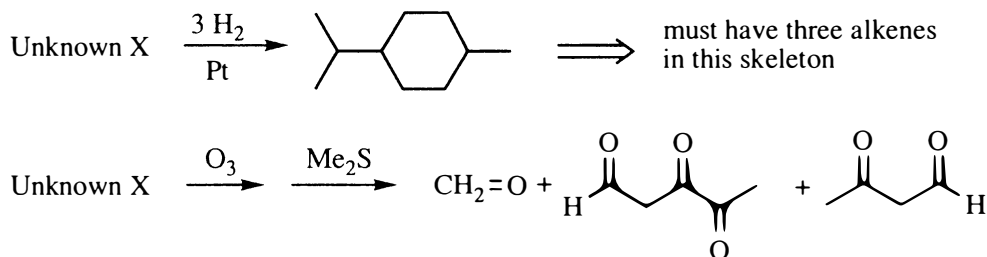
After ozonolysis, the two carbonyls are still connected; the alkene must have been in a ring, so reconnect the two carbonyl carbons with a double bond.



8-62 The two products from permanganate oxidation must have been connected by a double bond at the carbonyl carbons. Whether the alkene was *E* or *Z* cannot be determined by this experiment.

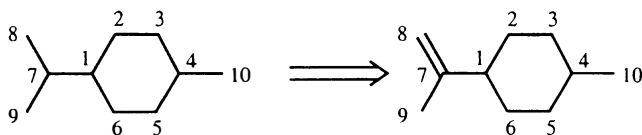


8-63

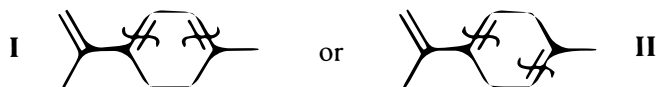


There are several ways to attack a problem like this. One is the trial-and-error method, that is, put double bonds in all possible positions until the ozonolysis products match. There are times when the trial-and-error method is useful (as in simple problems where the number of possibilities is few), but this is not one of them.

Let's try logic. Analyze the ozonolysis products carefully—what do you see? There are only two methyl groups, so one of the three terminal carbons in the skeleton (C-8, C-9, or C-10) has to be a $=\text{CH}_2$. Do we know which terminal carbon has the double bond? Yes, we can deduce that. If C-10 were double-bonded to C-4, then after ozonolysis, C-8 and C-9 must still be attached to C-7. However, in the ozonolysis products, there is no branched chain, that is, no combination of C-8 + C-9 + C-7 + C-1. What if C-7 had a double bond to C-1? Then we would have acetone, CH_3COCH_3 , as an ozonolysis product—we don't. Thus, we can't have a double bond from C-4 to C-10. One of the other terminal carbons (C-8) must have a double bond to C-7.



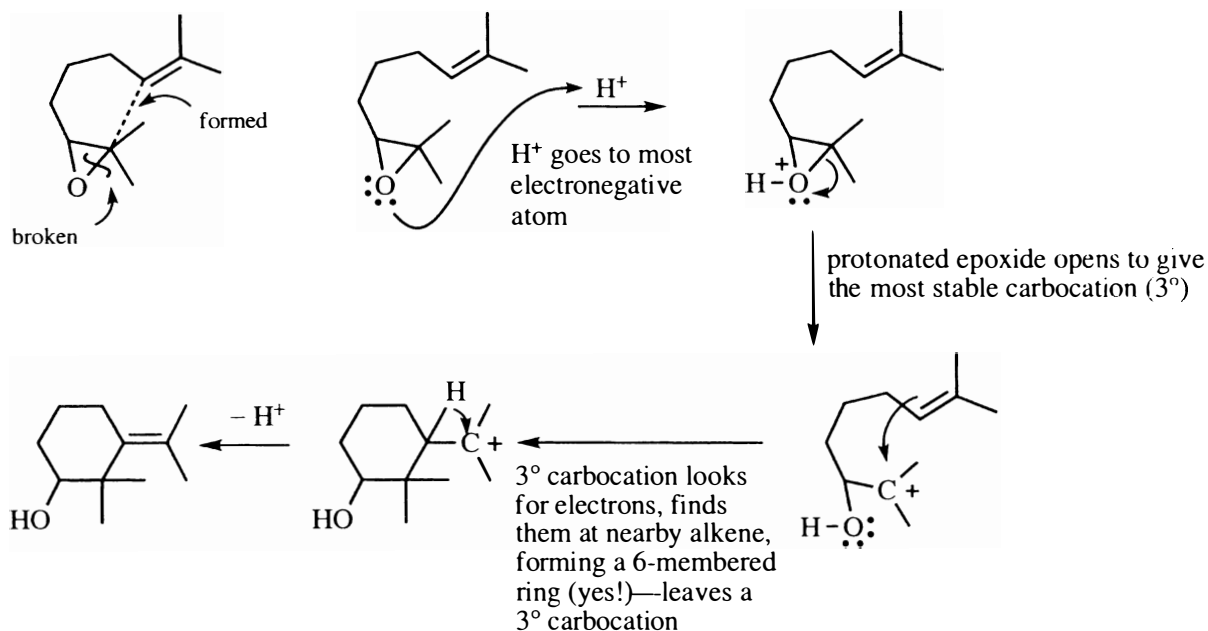
The other two double bonds have to be in the ring, but where? The products do not have branched chains, so double bonds must appear at both C-1 and C-4. There are only two possibilities for this requirement.



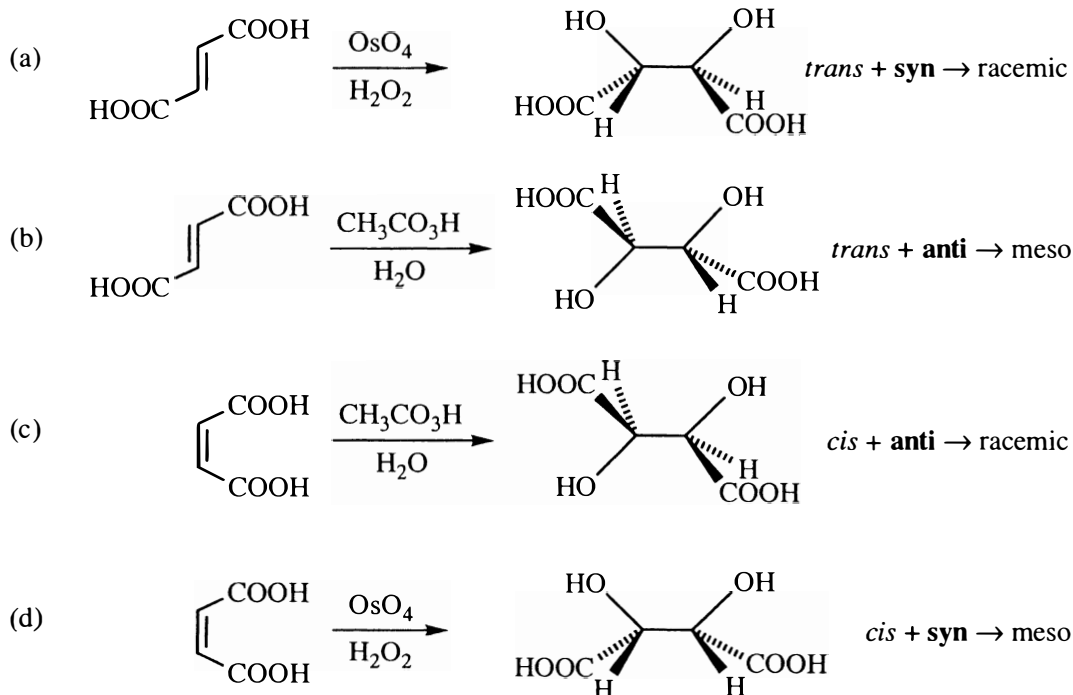
Ozonolysis of **I** would give fragments containing one carbon, two carbons, and seven carbons. Ozonolysis of **II** would give fragments containing one carbon, four carbons, and five carbons. Aha! Our mystery structure must be **II**.

(Editorial comment: Science is more than a collection of facts. The application of observation and logic to solve problems by *deduction* and *inference* are critical scientific skills, ones that distinguish humans from algae.)

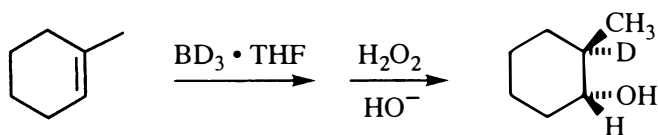
8-64 In this type of problem, begin by determining which bonds are broken and which are formed. These will always give clues as to what is happening.



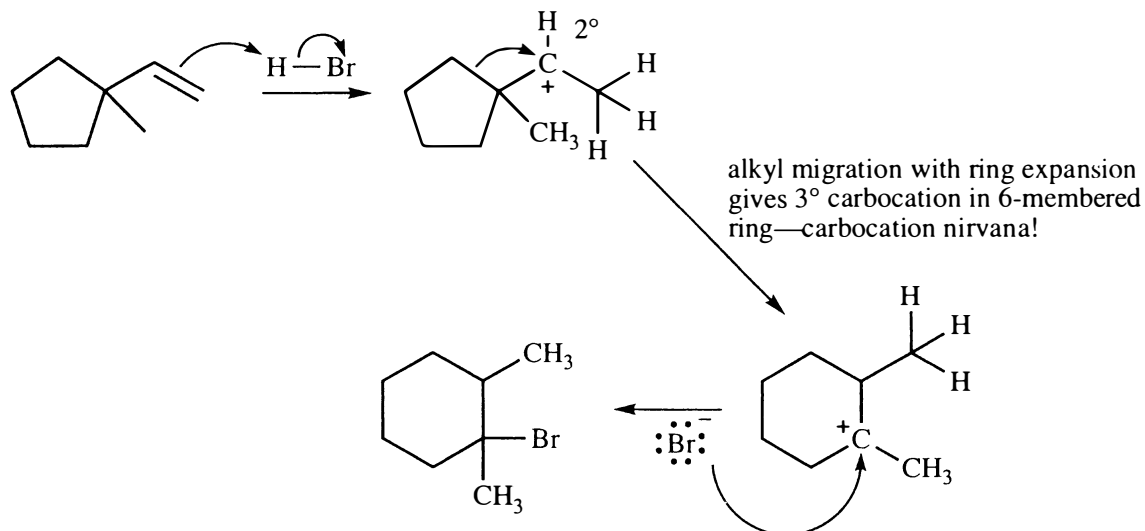
8-65 See the solution to Problem 8-35 for simplified examples of these reactions.



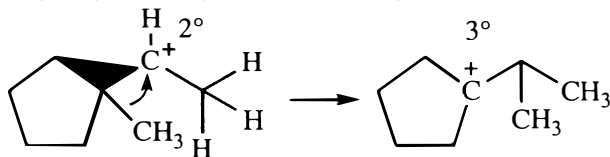
8-66



8-67 By now, these rearrangements should not be so "unexpected".

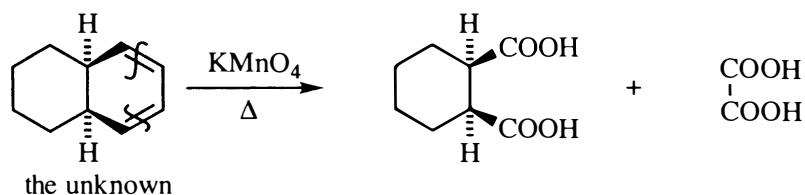


You must be asking yourself, "Why didn't the methyl group migrate?" To which you answered by drawing the carbocation that would have been formed:



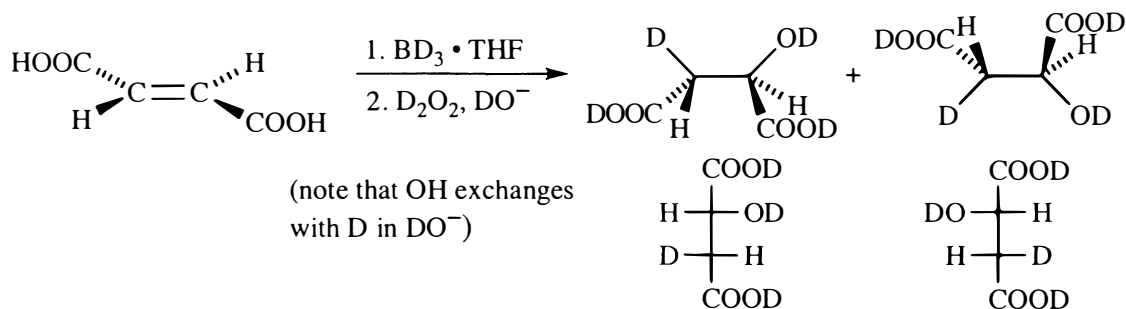
The new carbocation is indeed 3° , but it is only in a 5-membered ring, not quite as stable as in a 6-membered ring. In all probability, some of the product from methyl migration would be formed, but the 6-membered ring would be the major product.

8-68 Each alkene will produce two carbonyls upon ozonolysis or permanganate oxidation. Oxidation of the unknown generated four carbonyls, so the unknown must have had two alkenes. There is only one possibility for their positions.



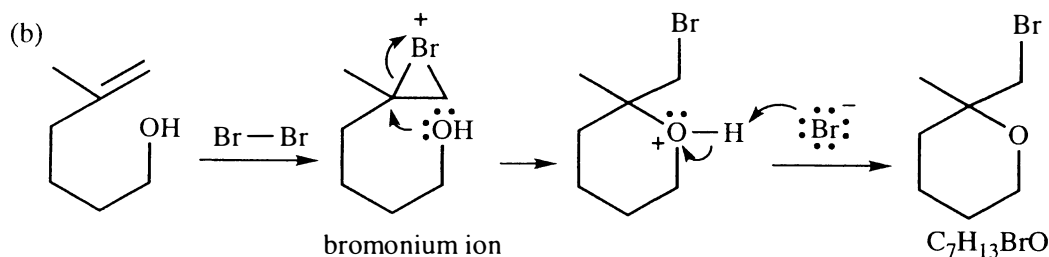
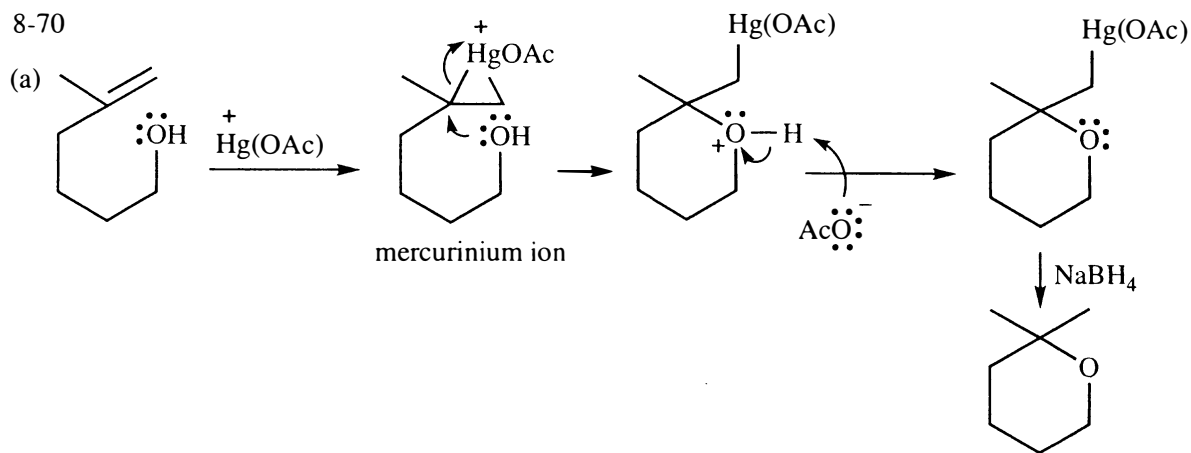
8-69

- (a) Fumarase catalyzes the addition of H and OH, a hydration reaction.
 (b) Fumaric acid is planar and cannot be chiral. Malic acid does have a chiral center and is chiral. The enzyme-catalyzed reaction produces only the *S* enantiomer, so the product must be optically active.
 (c) One of the fundamental rules of stereochemistry is that optically inactive starting materials produce optically inactive products. Sulfuric-acid-catalyzed hydration would produce a racemic mixture of malic acid, that is, equal amounts of *R* and *S*.
 (d) If the product is optically active, then either the starting materials or the catalyst were chiral. We know that water and fumaric acid are not chiral, so we must infer that fumarase is chiral.
 (e) The D and the OD are on the "same side" of the Fischer projection (sometimes called the "erythro" stereoisomer). These are produced from either: (1) syn addition to *cis* alkenes, or (2) anti addition to *trans* alkenes. We know that fumaric acid is *trans*, so the addition of D and OD must necessarily be anti.
 (f) Hydroboration is a syn addition.

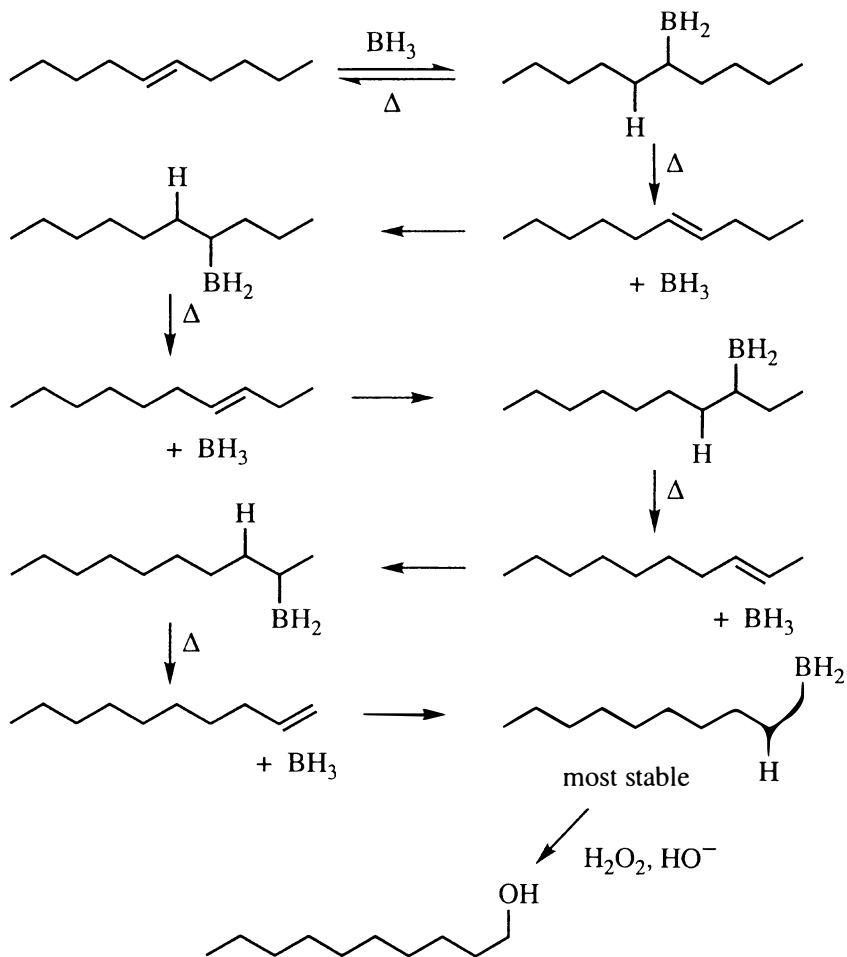


As expected, *trans* alkene plus syn addition puts the two groups on the "opposite" side of the Fischer projection (sometimes called "threo").

8-70

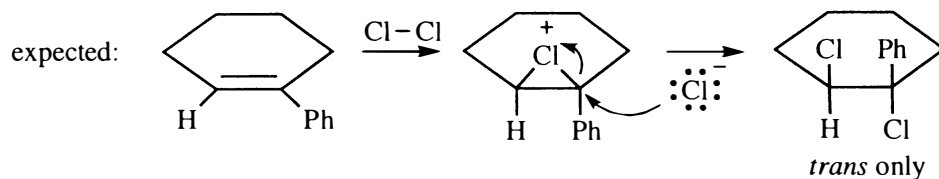


8-71 The addition of BH_3 to an alkene is reversible. Given heat and time, the borane will eventually "walk" its way to the end of the chain through a series of addition-elimination cycles. The most stable alkylborane has the boron on the end carbon; eventually, the series of equilibria lead to that product which is oxidized to the primary alcohol.

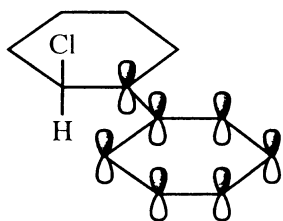
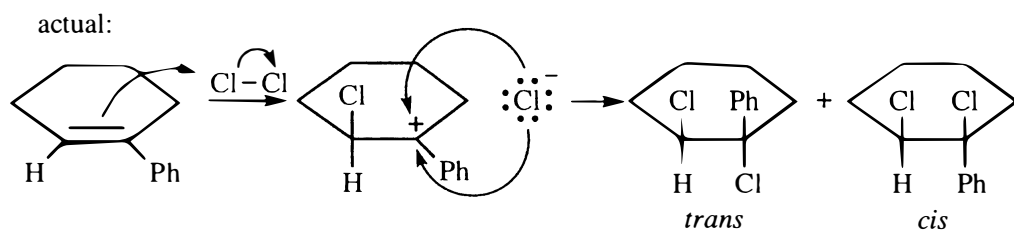


8-72 First, we explain *how* the mixture of stereoisomers results, then *why*.

We have seen many times that the bridged halonium ion permits attack of the nucleophile only from the opposite side.

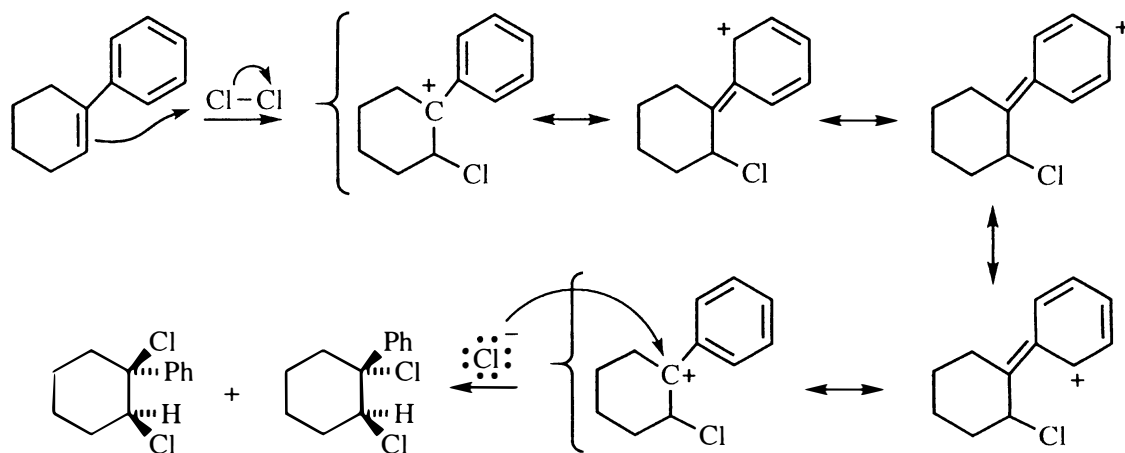


A mixture of *cis* and *trans* could result only if attack of chloride were possible from both top and bottom, something possible only if a *carbocation* existed at this carbon.



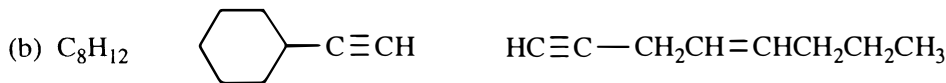
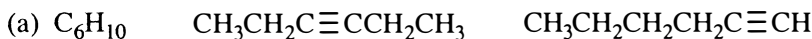
This picture of the p orbitals of benzene show resonance overlap with the p orbital of the carbocation. The chloride nucleophile can form a bond to the positive carbon from either the top or the bottom.

Why does a carbocation exist here? Not only is it 3°, it is also *next to a benzene ring (benzylic)* and therefore *resonance-stabilized*. This resonance stabilization would be forfeited in a halonium ion intermediate.

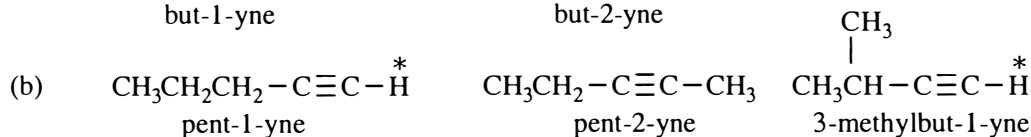
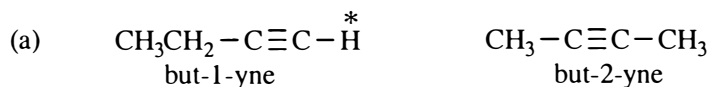


CHAPTER 9—ALKYNES

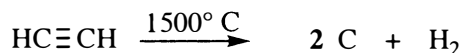
9-1 Other structures are possible in each case.



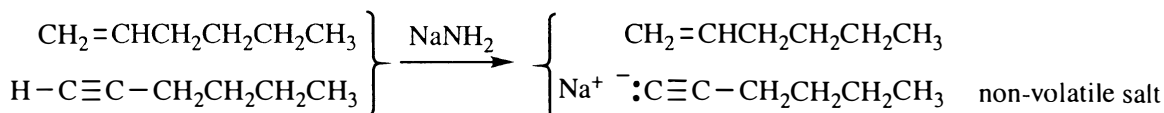
9-2 New IUPAC names are given. The asterisk (*) denotes acetylenic hydrogens of terminal alkynes.



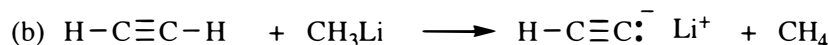
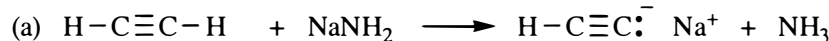
9-3 The decomposition reaction below is exothermic ($\Delta H^\circ = -234$ kJ/mole) as well as having an increase in entropy. Thermodynamically, at $1500^\circ C$, an increase in entropy will have a large effect on ΔG (remember $\Delta G = \Delta H - T\Delta S$). Kinetically, almost any activation energy barrier will be overcome at $1500^\circ C$. Acetylene would likely decompose into its elements:



9-4 Adding sodium amide to the mixture will produce the sodium salt of hex-1-yne, leaving hex-1-ene untouched. Distillation will remove the hex-1-ene, leaving the non-volatile salt behind.



9-5 The key to this problem is to understand that *a proton donor will react only with the conjugate base of a weaker acid*. See Appendix 2 at the end of this Solutions Manual for an in-depth discussion of acidity.



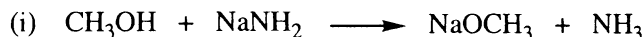
(c) no reaction: $NaOCH_3$ is not a strong enough base

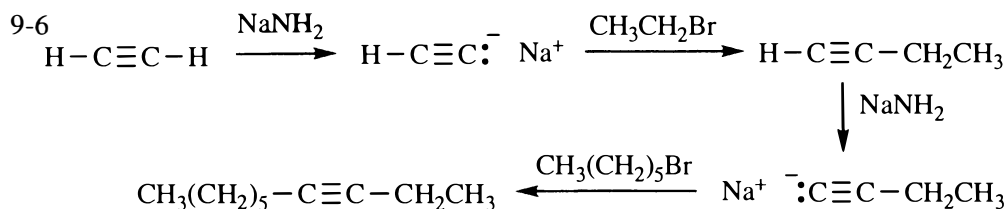
(d) no reaction: $NaOH$ is not a strong enough base



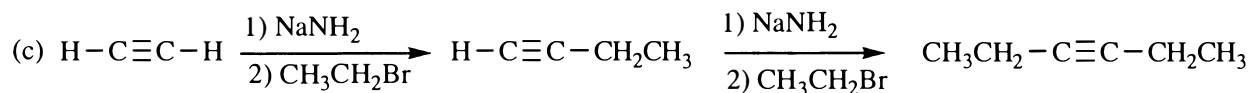
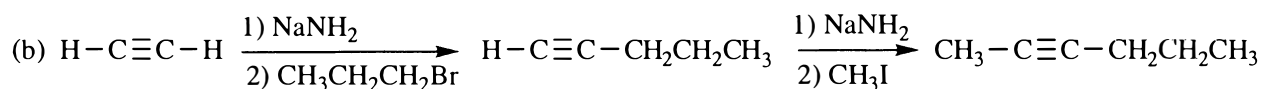
(g) no reaction: $H-C\equiv C:\text{ } ^- Na^+$ is not a strong enough base

(h) no reaction: $NaNH_2$ is not a strong enough base

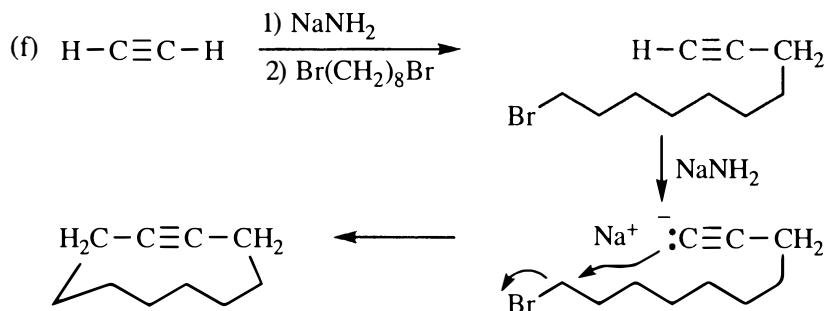
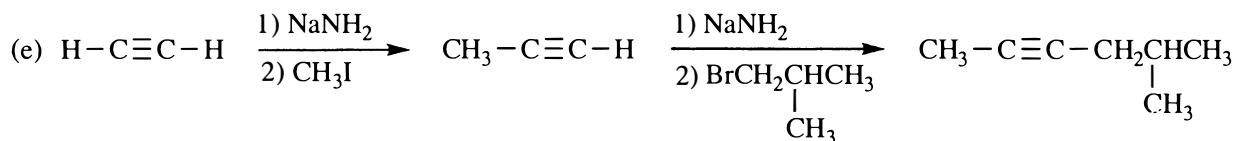
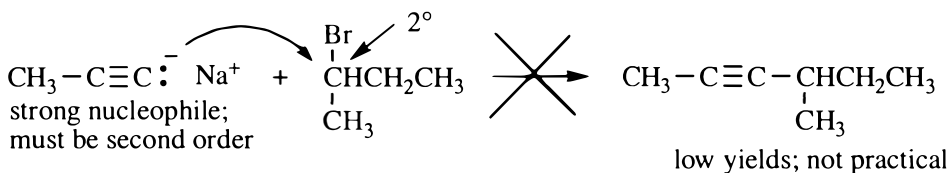




9-7

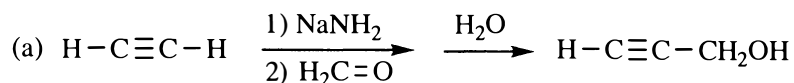


(d) cannot be synthesized by an $\text{S}_{\text{N}}2$ reaction—would require attack on a 2° alkyl halide

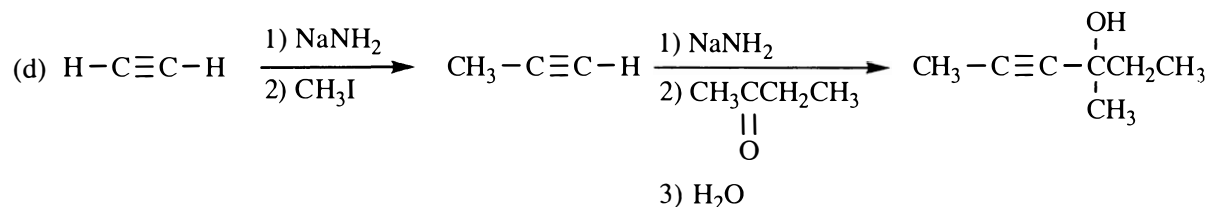
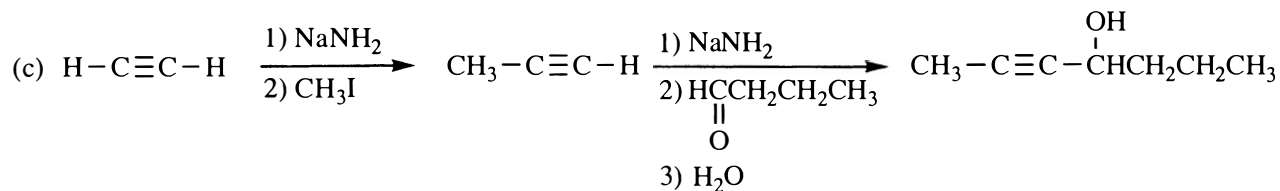
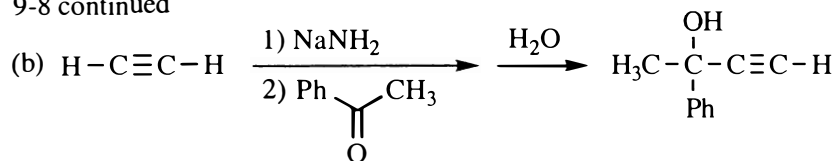


Intramolecular cyclization of large rings must be carried out in dilute solution so the last $\text{S}_{\text{N}}2$ displacement will be *intramolecular* and not *intermolecular*.

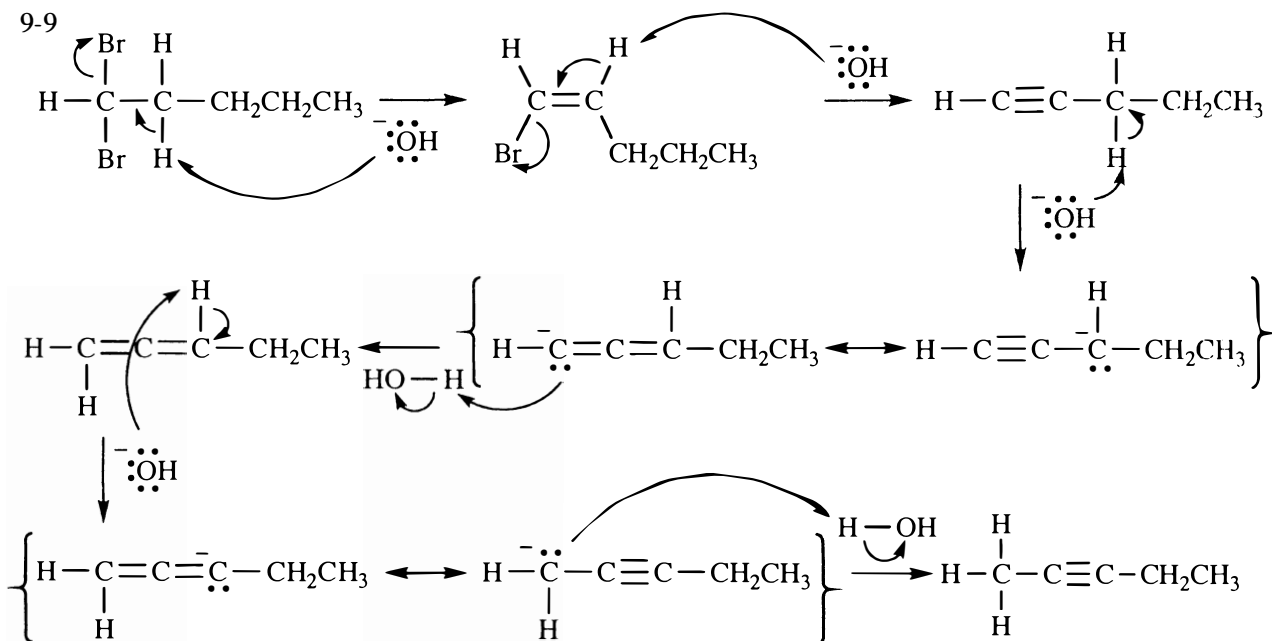
9-8



9-8 continued



9-9



9-10 To determine the equilibrium constant in the reaction:

terminal alkyne $\rightleftharpoons$ internal alkyne

$$\Delta G = -17.0 \text{ kJ/mole}$$

$$(-4.0 \text{ kcal/mole})$$

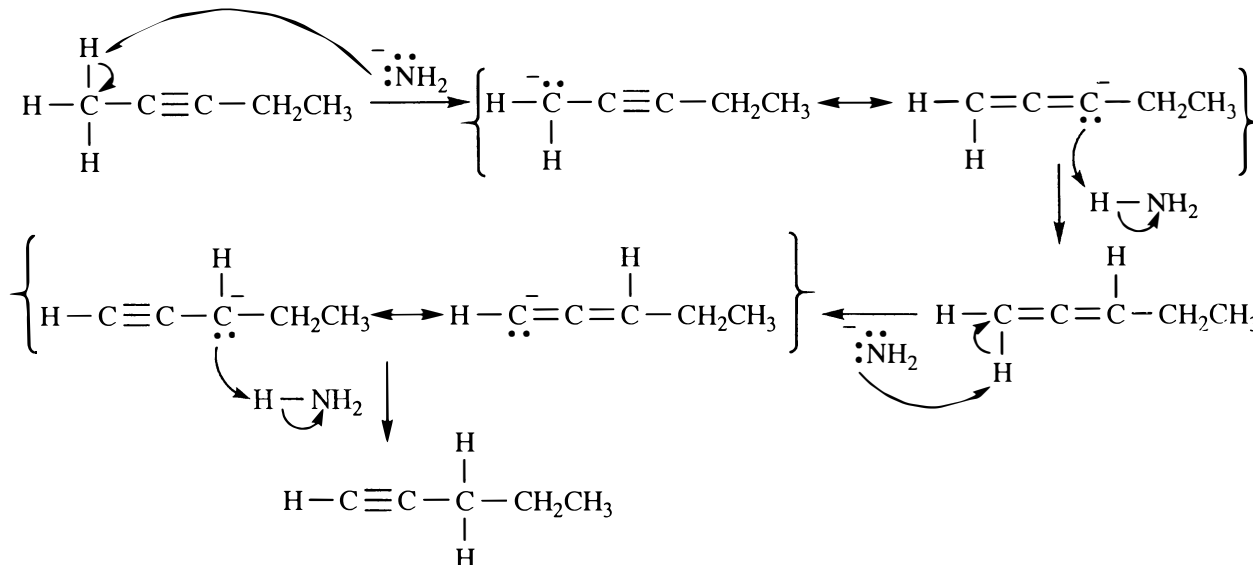
$$R = 8.314 \text{ J/K}\cdot\text{mole}$$

$$\Delta G = -RT \ln K_{\text{eq}}$$

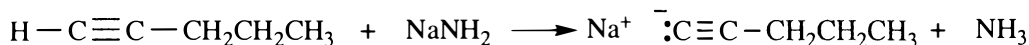
$$K_{\text{eq}} = e^{\left(-\frac{\Delta G}{RT}\right)} = e^{\left(\frac{-(-17,000)}{(8.314)(473)}\right)} = e^{4.32} = 75$$

$$\frac{[\text{internal}]}{[\text{terminal}]} = \frac{75}{1} = \frac{98.7\% \text{ internal}}{1.3\% \text{ terminal}}$$

9-11 (a) This isomerization is the reverse of the mechanism in the solution to 9-9.



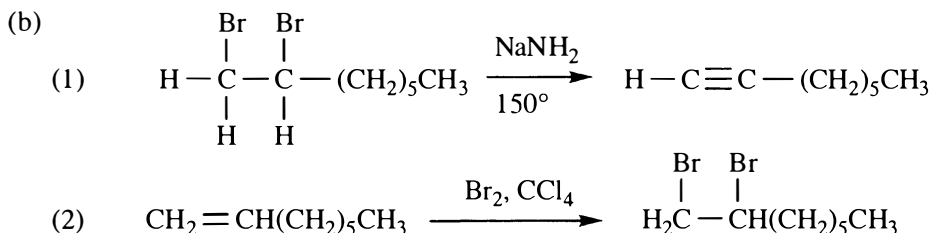
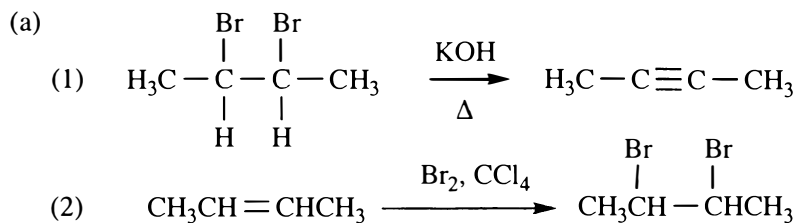
(b) All steps in part (a) are reversible. With a weaker base like KOH, an equilibrium mixture of pent-1-yne and pent-2-yne would result. With the strong base NaNH_2 , however, the final terminal alkyne is deprotonated to give the acetylide ion:



Because pent-1-yne is about 10 pK units more acidic than ammonia, this deprotonation is *not reversible*. The acetylide ion is produced and can't go back. Le Châtelier's Principle tells us that the reaction will try to replace the pent-1-yne that is being removed from the reaction mixture, so eventually all of the pent-2-yne will be drawn into the pent-1-yne anion "sink".

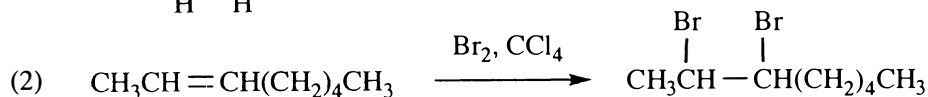
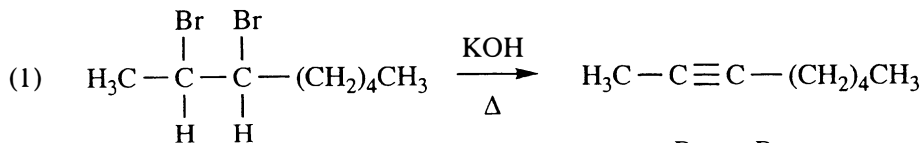
(c) Using the weaker base KOH at 200°C will restore the equilibrium between the two alkyne isomers with pent-2-yne predominating.

9-12

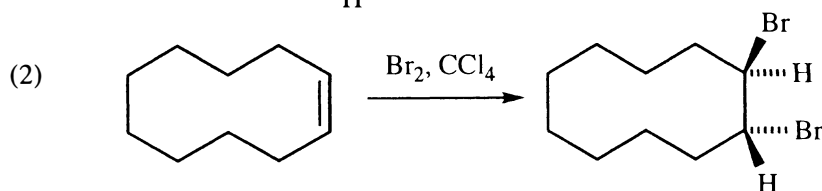
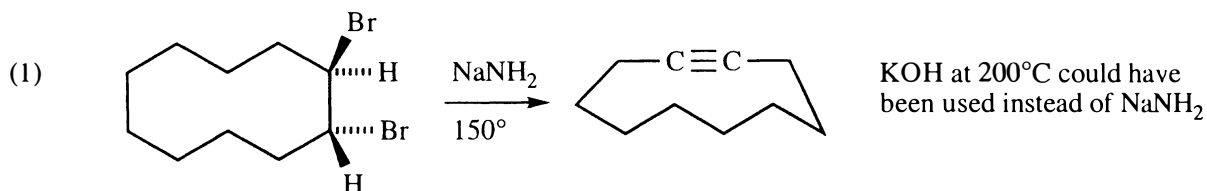


9-12 continued

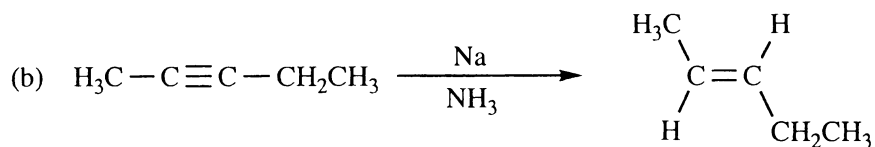
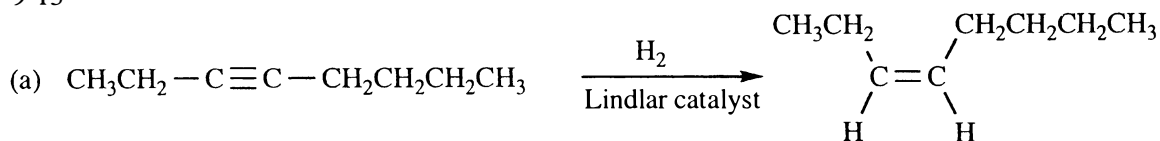
(c)



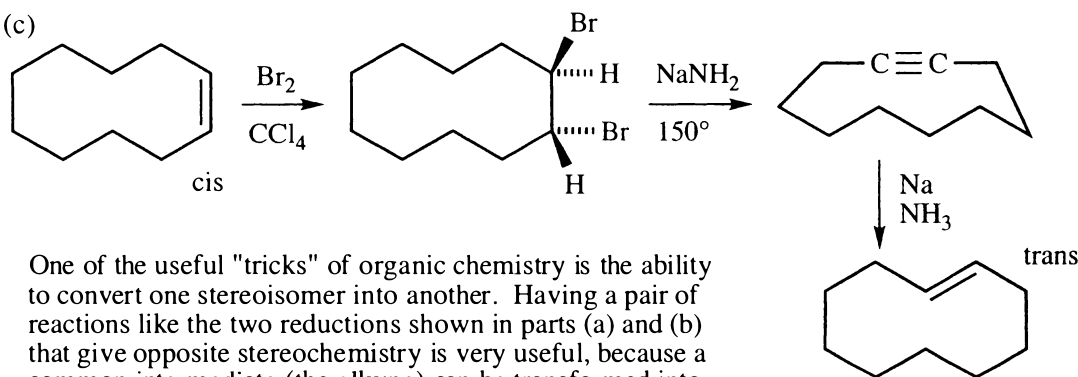
(d)



9-13

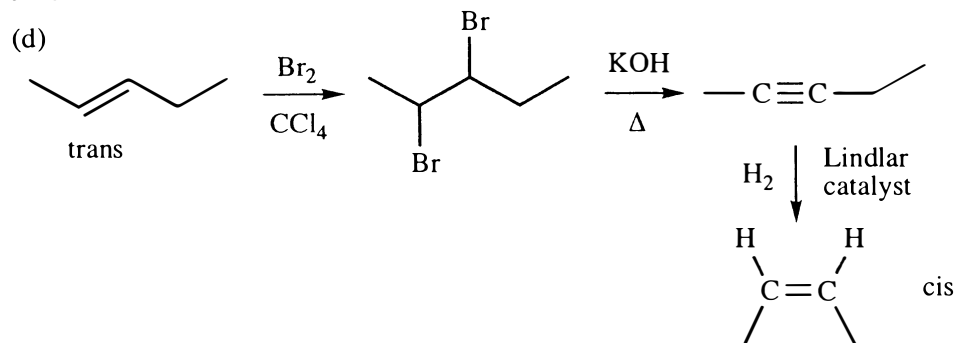


(c)

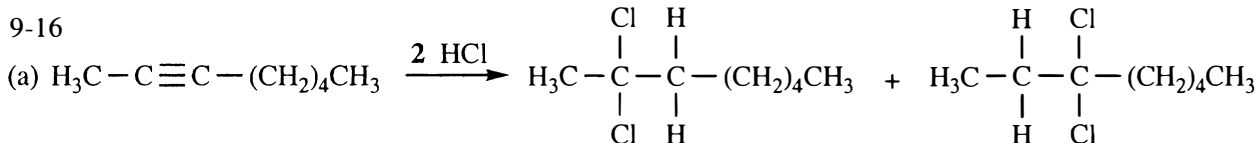
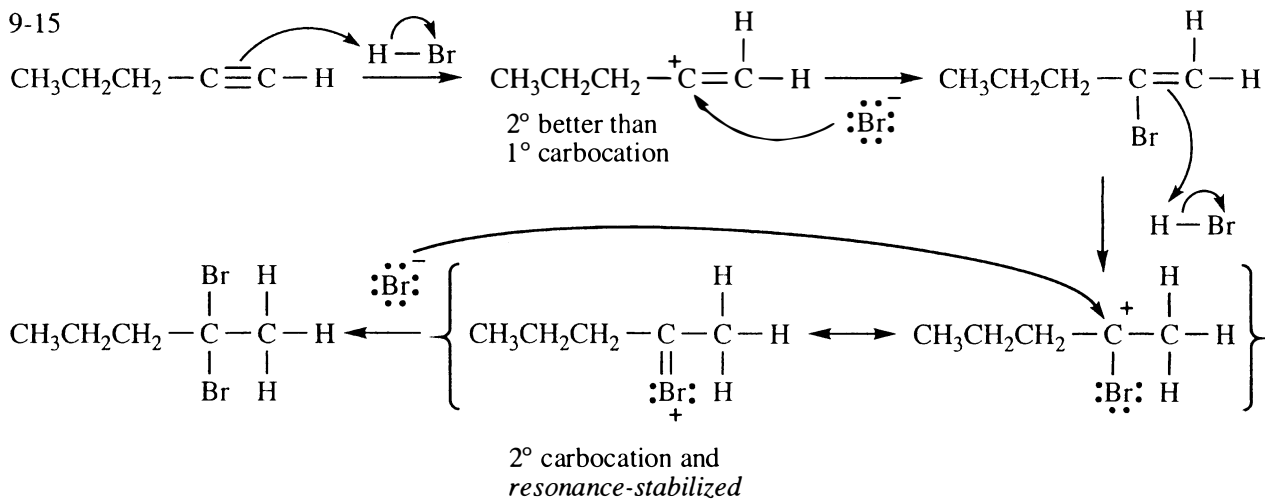


One of the useful "tricks" of organic chemistry is the ability to convert one stereoisomer into another. Having a pair of reactions like the two reductions shown in parts (a) and (b) that give opposite stereochemistry is very useful, because a common intermediate (the alkyne) can be transformed into either stereoisomer. This principle is used again in part (d).

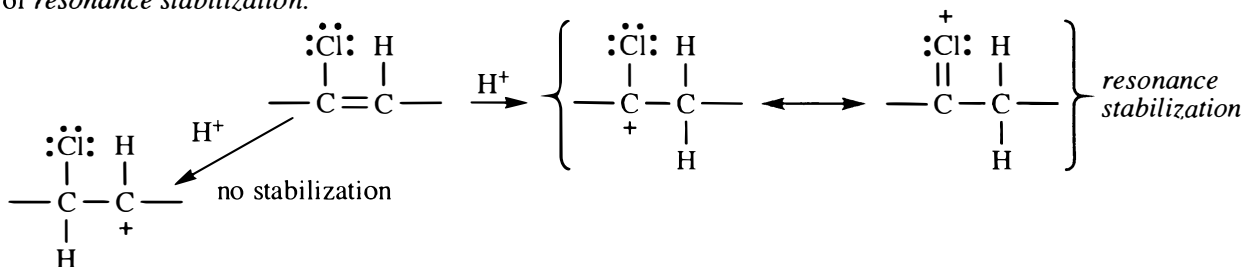
9-13 continued



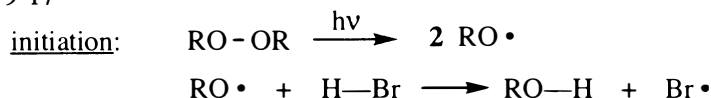
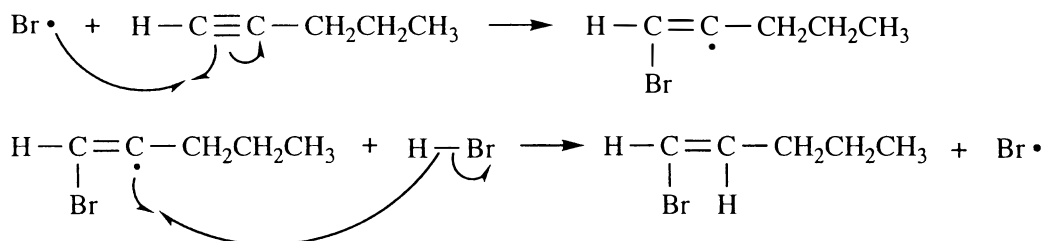
9-14 The goal is to add only one equivalent of bromine, always avoiding an excess of bromine, because two molecules of bromine could add to the triple bond if bromine was in excess. If the alkyne is added to the bromine, the first drops of alkyne will encounter a large excess of bromine. Instead, adding bromine to the alkyne will always ensure an excess of alkyne and should give a good yield of dibromo product.



(b) The second addition occurs to make the carbocation intermediate at the carbon with the halogen because of *resonance stabilization*.

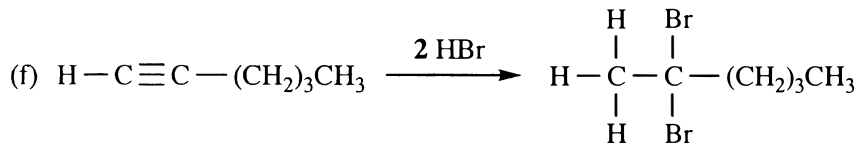
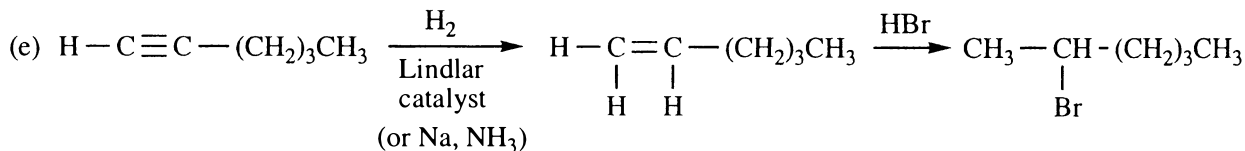
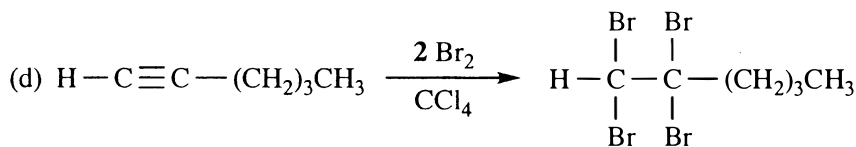
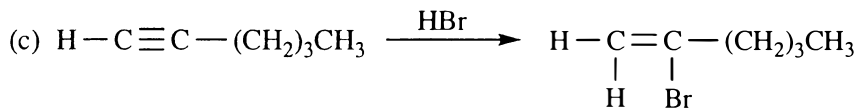
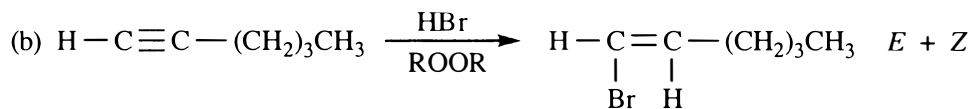
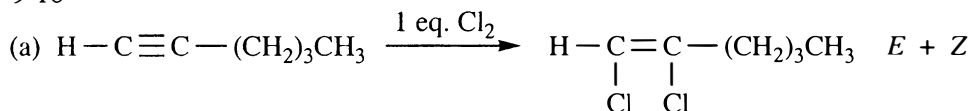


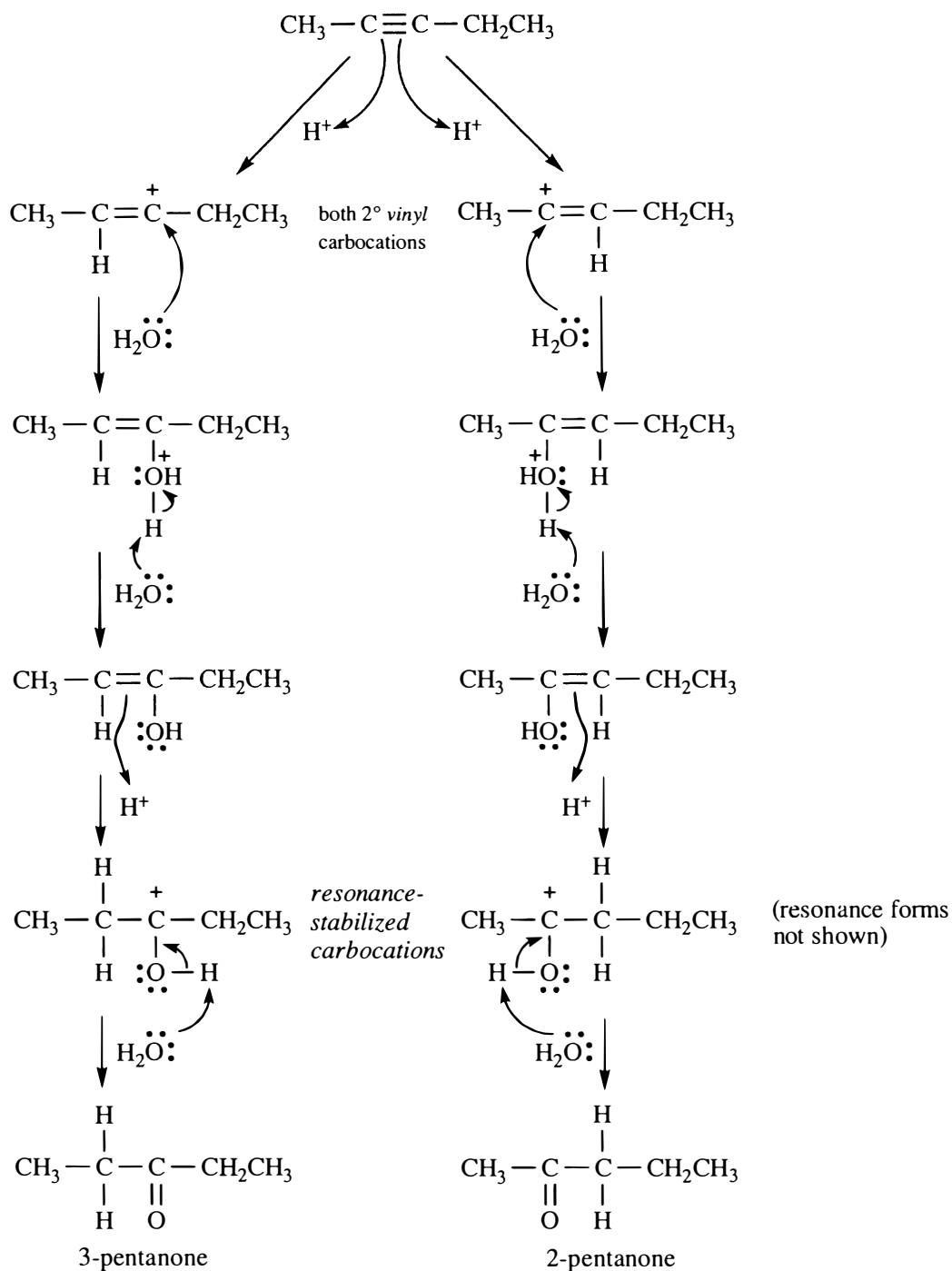
9-17

propagation:

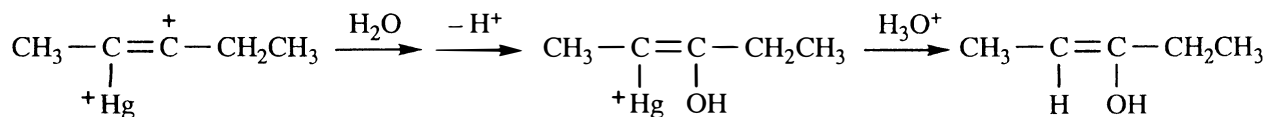
The 2° radical is more stable than 1°. The anti-Markovnikov orientation occurs because the bromine radical attacks first to make the most stable radical, which is contrary to electrophilic addition where the H^+ attacks first (see the solution to 9-15).

9-18



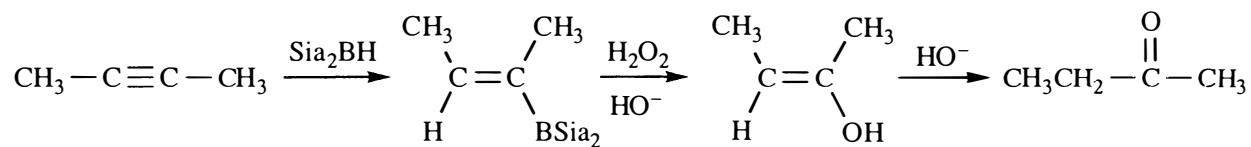


The role of the mercury catalyst is not shown in this mechanism. As a Lewis acid, it may act like the proton in the first step, helping to form vinyl cations; the mercury is replaced when acid is added.

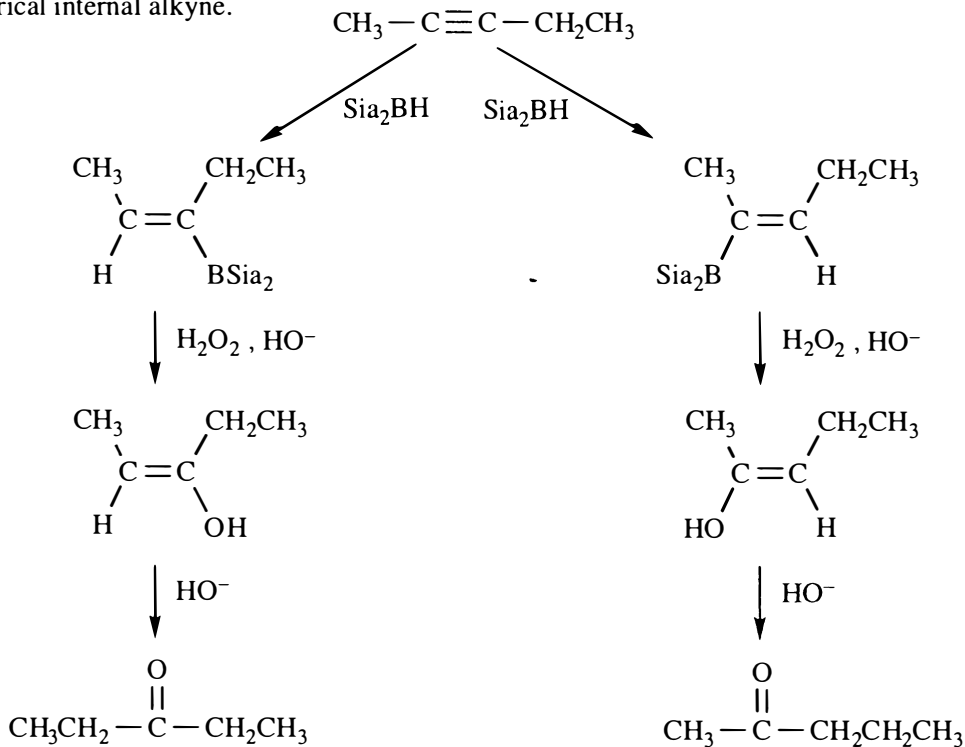


9-20

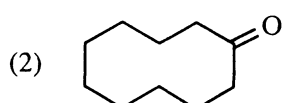
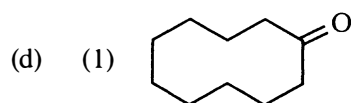
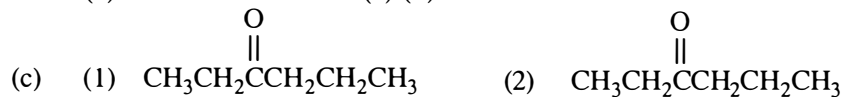
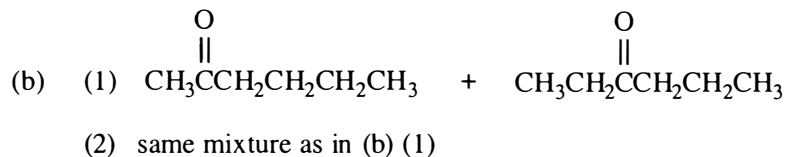
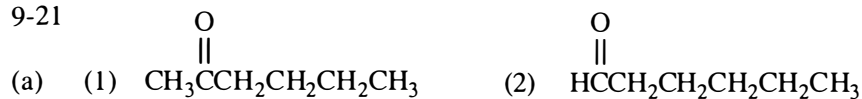
(a) But-2-yne is symmetric. Either orientation produces the same product.



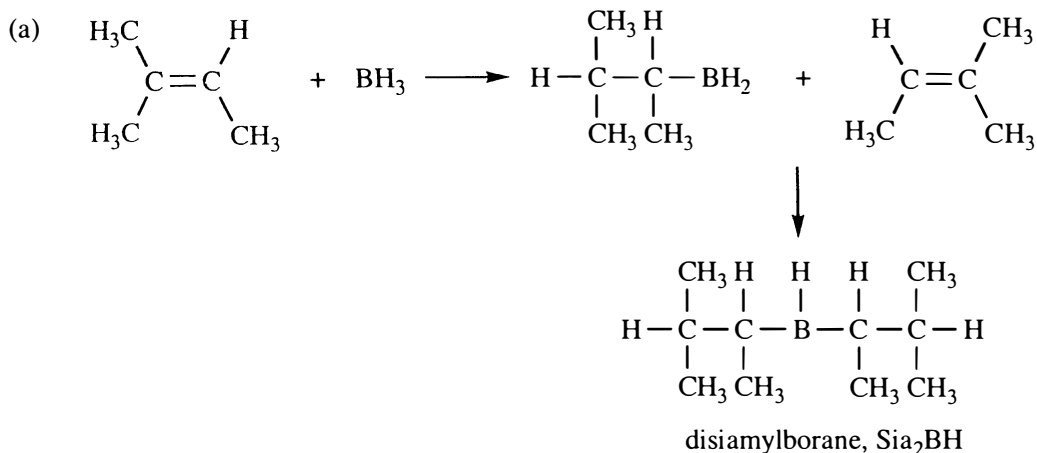
(b) Pent-2-yne is not symmetric. Different orientations of attack will lead to different products on any unsymmetrical internal alkyne.



9-21

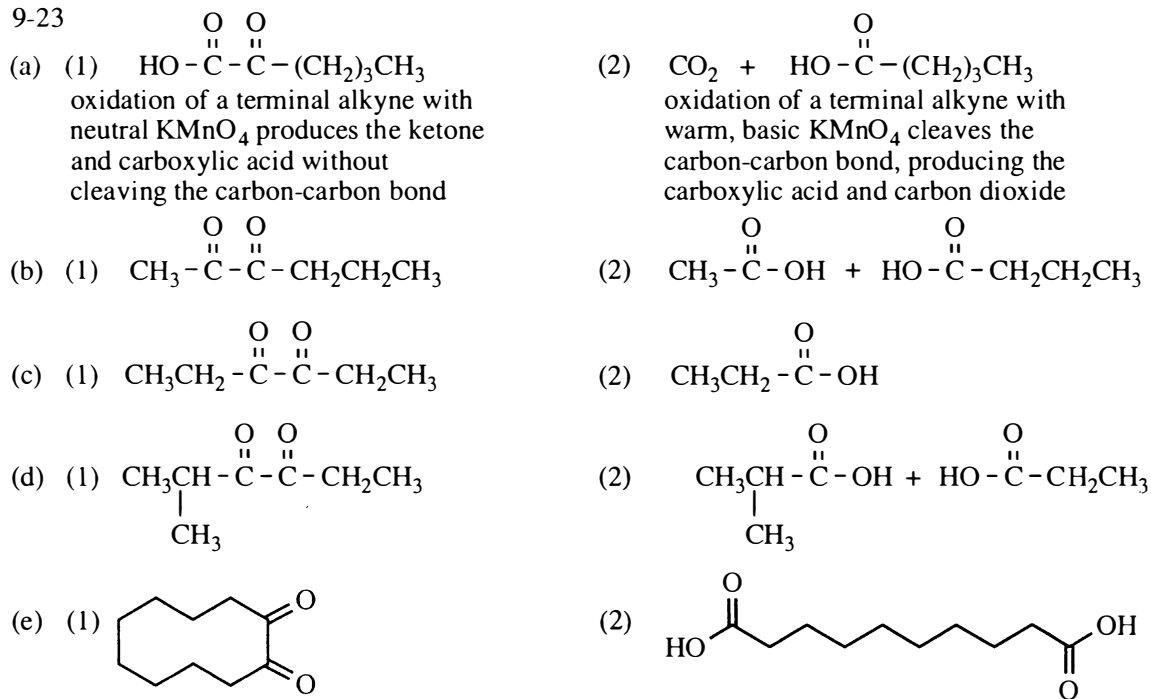


9-22

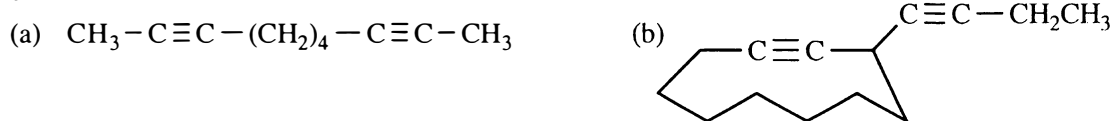


(b) There is too much steric hindrance in Sia_2BH for the third B—H to add across another alkene. The reagent can add to alkynes because alkynes are linear and attack is not hindered by bulky substituents.

9-23



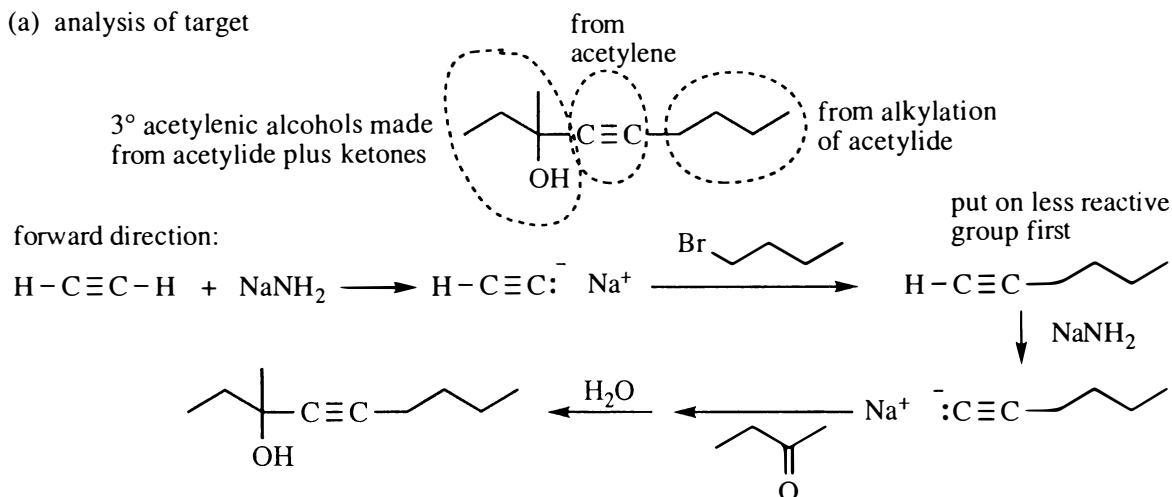
9-24

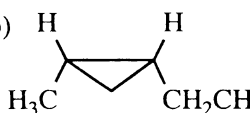


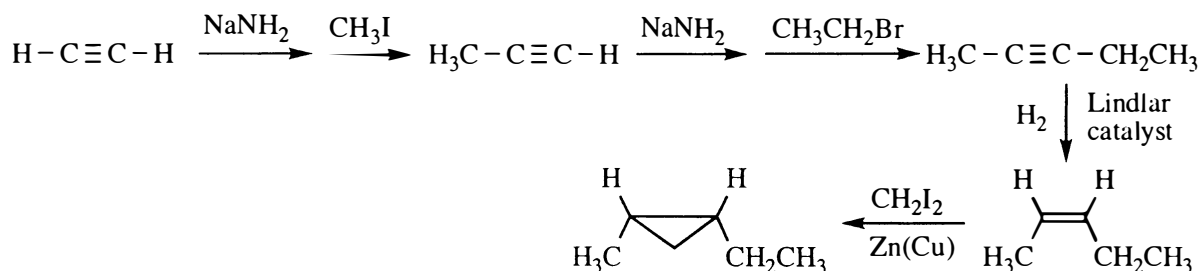
9-25 When proposing syntheses, begin by analyzing the target molecule, looking for smaller pieces that can be combined to make the desired compound. This is especially true for targets that have more carbons than the starting materials; immediately, you will know that a carbon-carbon bond forming reaction will be necessary.

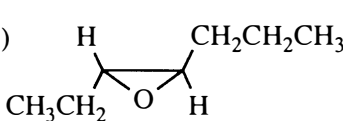
People who succeed at synthesis *know the reactions*—there is no shortcut. Practice the reactions for each functional group until they become automatic.

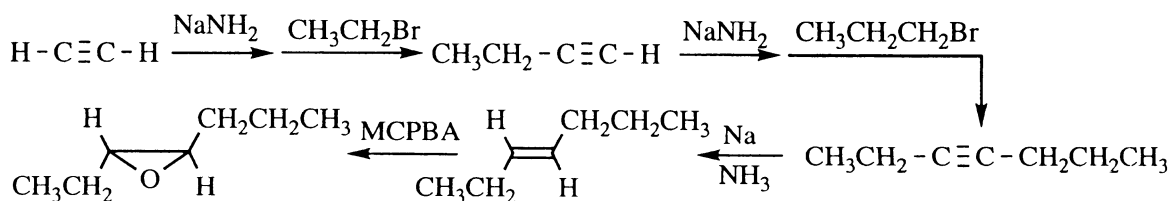
(a) analysis of target



(b)  analysis of target: cyclopropanes are made by carbene insertion into alkenes; to get *cis* substitution around cyclopropane, stereochemistry of alkene must be *cis*; *cis* alkene comes from catalytic hydrogenation of an alkyne

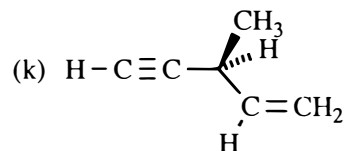
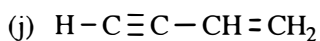
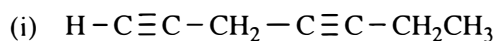
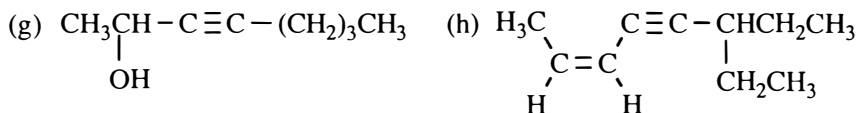
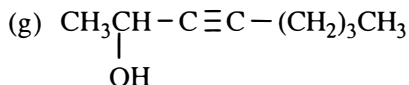
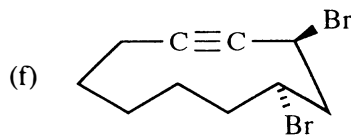
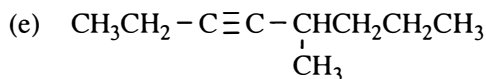
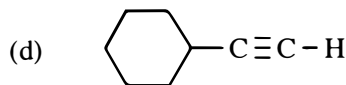
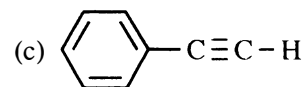
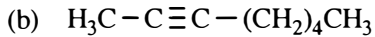
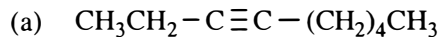


(c)  analysis of target: epoxides are made by direct epoxidation of alkenes; to get *trans* substitution around epoxide, stereochemistry of alkene must be *trans*; *trans* alkene comes from sodium/ammonia reduction of an alkyne



9-26 Please refer to solution 1-20, page 12 of this Solutions Manual.

9-27



9-28

(a) ethylmethylacetylene

(c) *sec*-butyl-*n*-propylacetylene

(b) phenylacetylene

(d) *sec*-butyl-*t*-butylacetylene

9-29

(a) 4-phenylpent-2-yne

(c) 2,6,6-trimethylhept-3-yne

(e) 3-methylhex-4-yn-3-ol

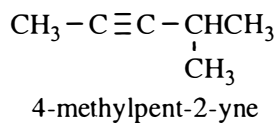
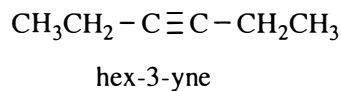
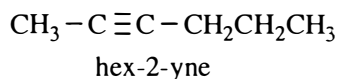
(b) 4,4-dibromopent-2-yne

(d) (*E*)-3-methylhept-2-en-4-yne

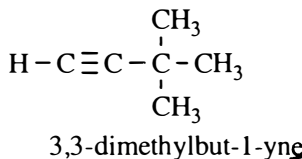
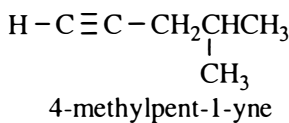
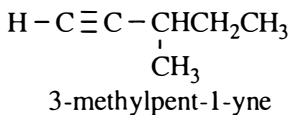
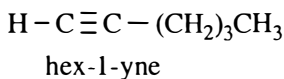
(f) cycloheptylprop-1-yne

9-30

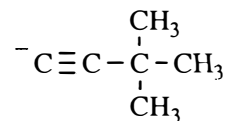
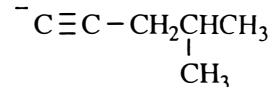
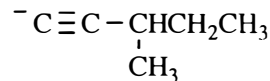
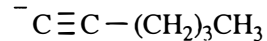
(a) internal alkynes



terminal alkynes



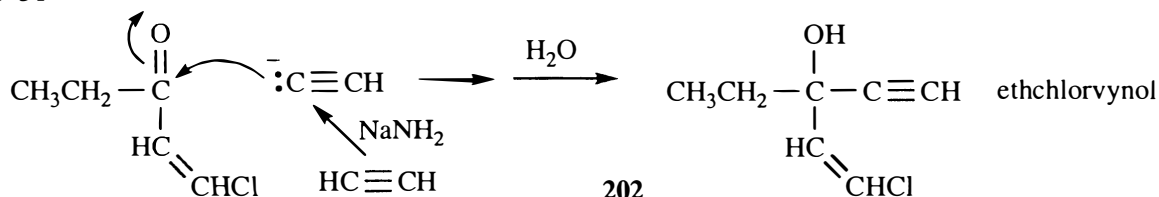
acetylide ions



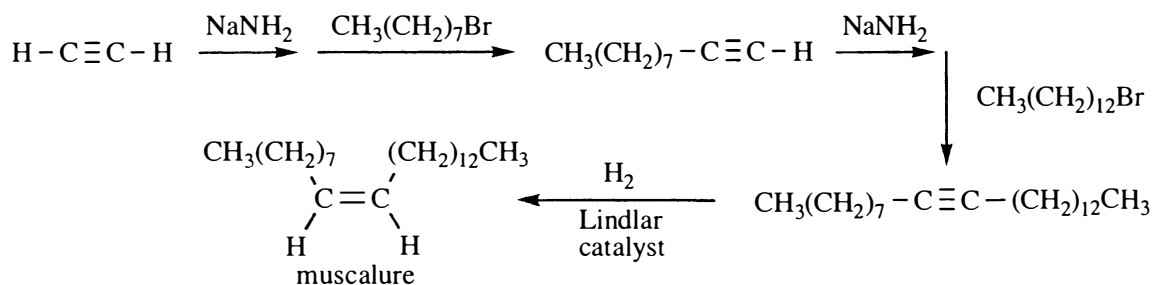
NaNH_2

(b) All four terminal alkynes will be deprotonated with sodium amide.

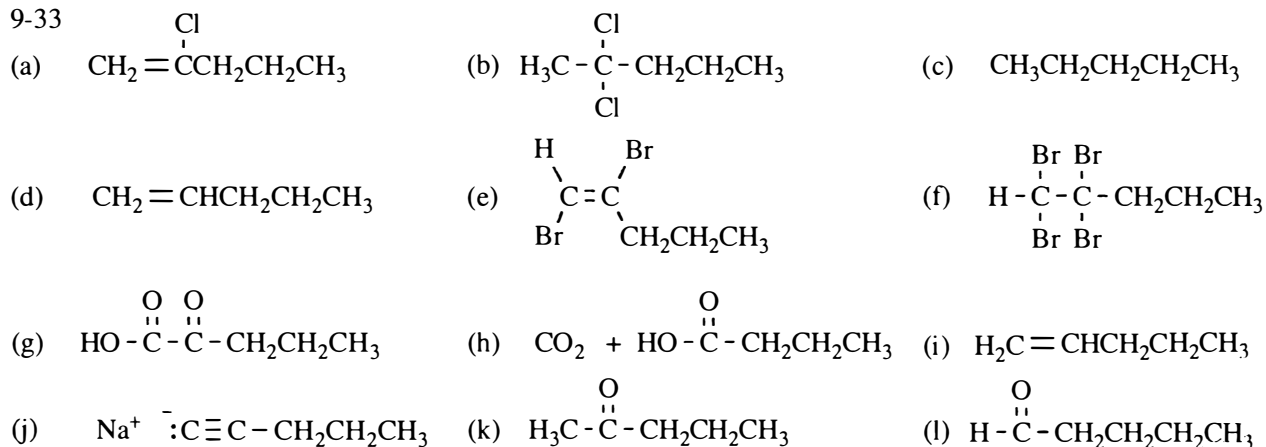
9-31



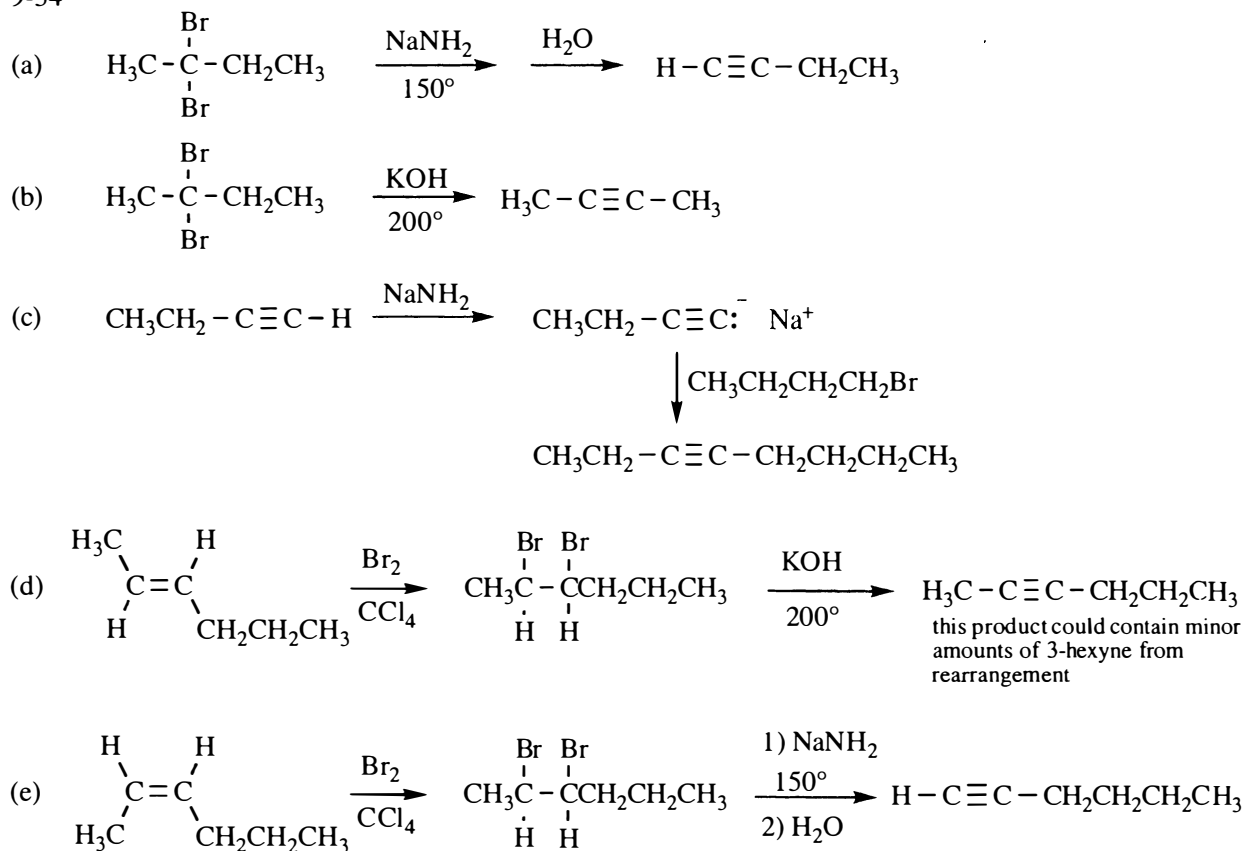
9-32



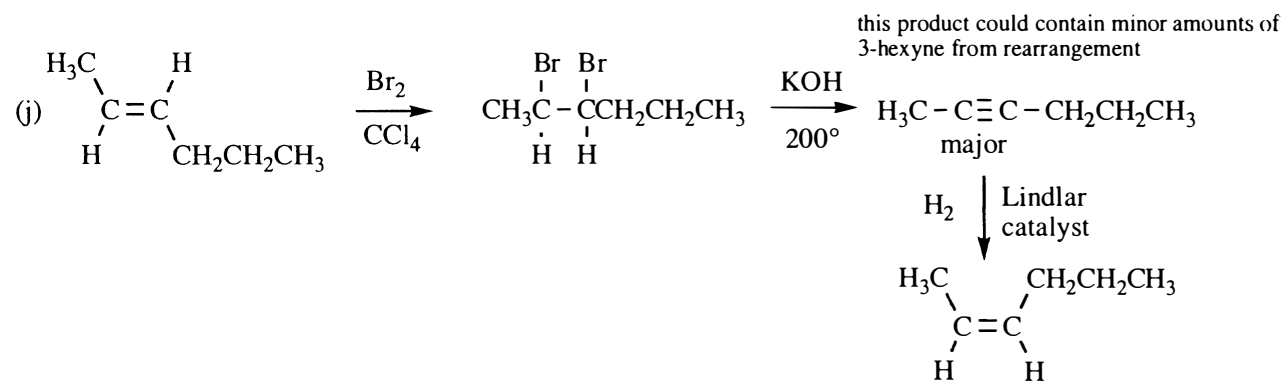
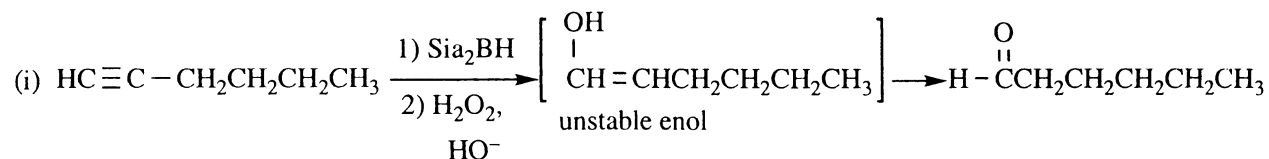
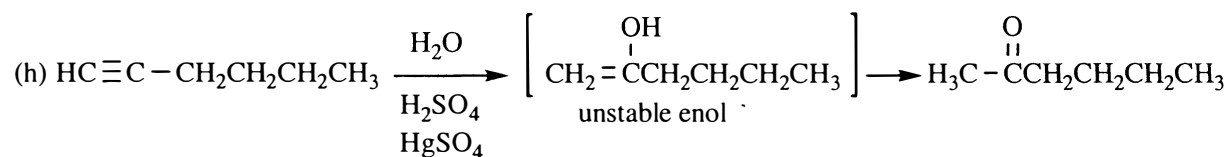
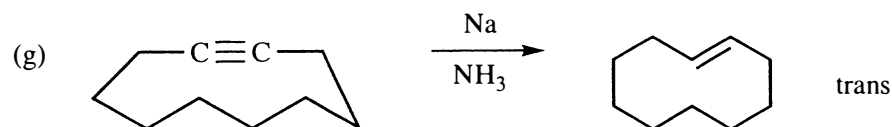
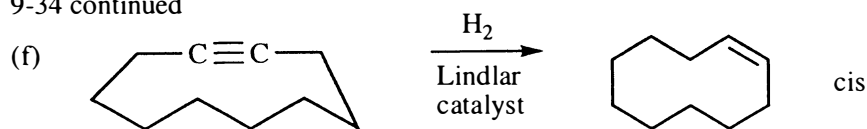
9-33



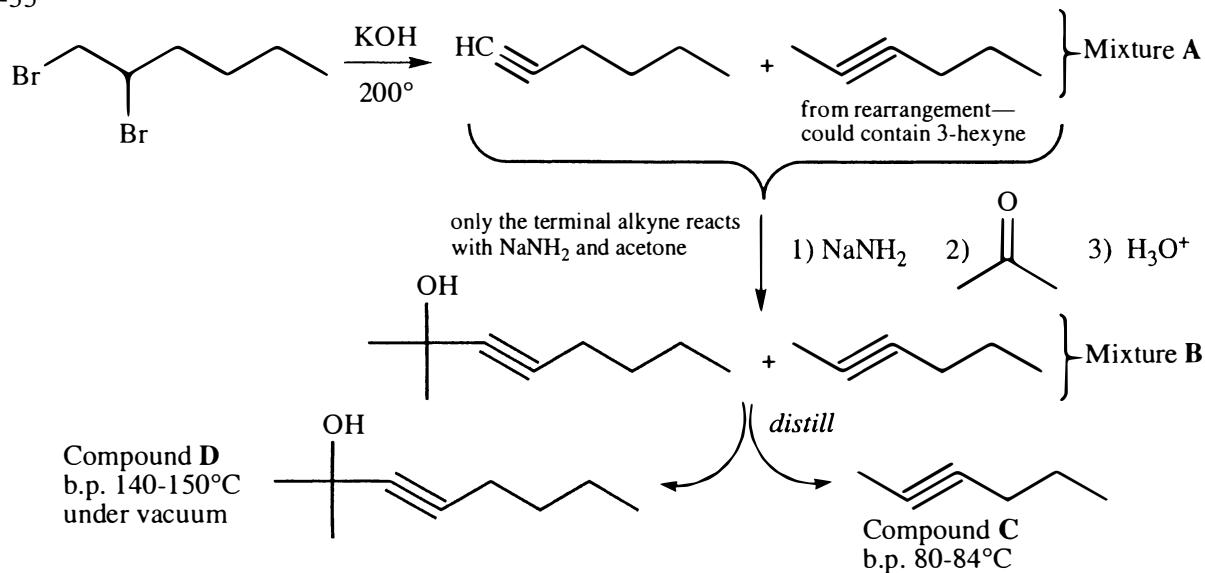
9-34



9-34 continued



9-35



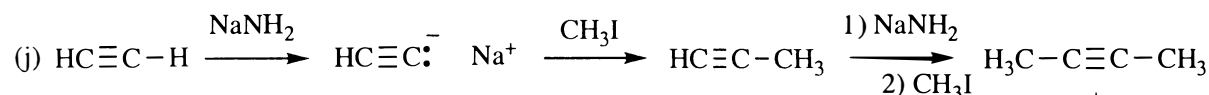
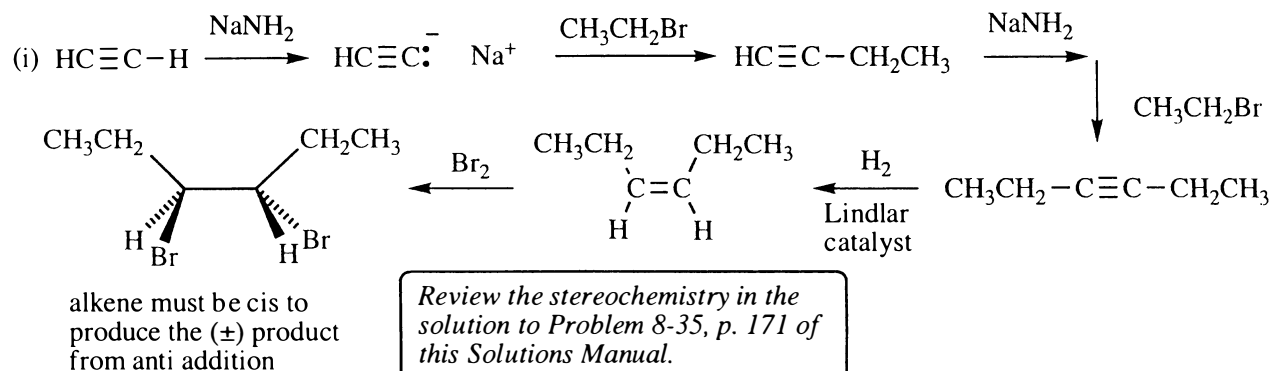
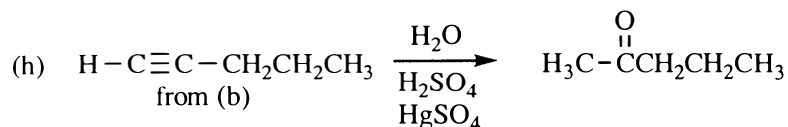
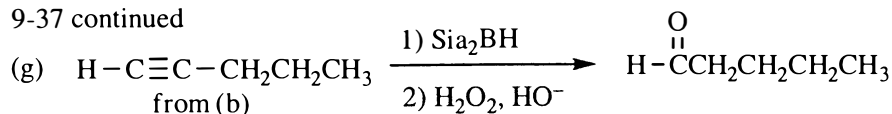
9-36

- (a) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$
- (b) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{H} + \text{CH}_2=\text{C}(\text{CH}_3)_2$ elimination on 3° halide
- (c) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}_2\text{OH}$
(after H_2O workup)
- (d) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{C}(\text{OH})(\text{CH}_2)_5\text{CH}_3$
(after H_2O workup)
- (e) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}(\text{OH})\text{CH}_2\text{CH}_2\text{CH}_3$
(after H_2O workup)
- (f) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{H} + \text{Na}^+ \text{ } ^-\text{O}-\text{C}_6\text{H}_{11}$
- (g) $\text{CH}_3\text{CH}_2-\text{C}\equiv\text{C}-\text{C}(\text{OH})(\text{CH}_3)\text{CH}_2\text{CH}_3$
(after H_2O workup)

9-37

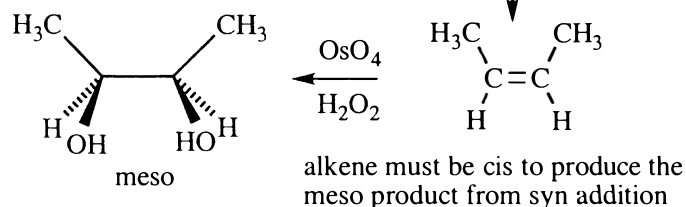
- (a) $\text{HC}\equiv\text{C}-\text{H} \xrightarrow{\text{NaNH}_2} \text{HC}\equiv\text{C}:^- \text{Na}^+ \xrightarrow{\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}} \text{HC}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$
- (b) $\text{HC}\equiv\text{C}-\text{H} \xrightarrow{\text{NaNH}_2} \text{HC}\equiv\text{C}:^- \text{Na}^+ \xrightarrow{\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}} \text{HC}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_3$
 $\downarrow \text{NaNH}_2$
 $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_3 \xleftarrow{\text{CH}_3\text{I}}$
- (c) $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow[\text{Lindlar catalyst}]{\text{H}_2} \text{H}_3\text{C}-\text{C}(\text{H})=\text{C}(\text{H})-\text{CH}_2\text{CH}_2\text{CH}_3$
synthesized in part (b)
- (d) $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow[\text{NH}_3]{\text{Na}} \text{H}_3\text{C}-\text{C}(\text{H})=\text{C}(\text{H})-\text{CH}_2\text{CH}_2\text{CH}_3$
synthesized in part (b)
- (e) $\text{H}_3\text{C}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow[\text{Pt}]{2 \text{ equiv. } \text{H}_2} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$
synthesized in part (b)
- (f) $\text{HC}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow{2 \text{ HBr}} \text{H}_3\text{C}-\text{C}(\text{Br})_2-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$
synthesized in part (a)

9-37 continued

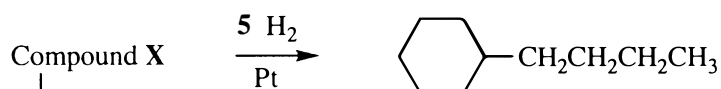


Alternatively, *trans*-but-2-ene could be anti-hydroxylated with aqueous peracetic acid.

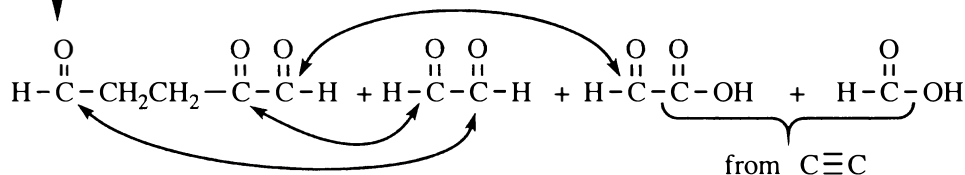
Review the stereochemistry in the solution to Problem 8-35, p. 171 of this Solutions Manual.



9-38

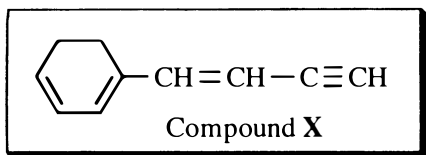


the fact that five equivalents of hydrogen are consumed says that X must have five pi bonds in the above carbon skeleton

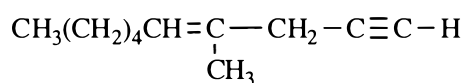
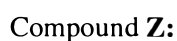


6 carbonyls $\Rightarrow$ 3 alkenes

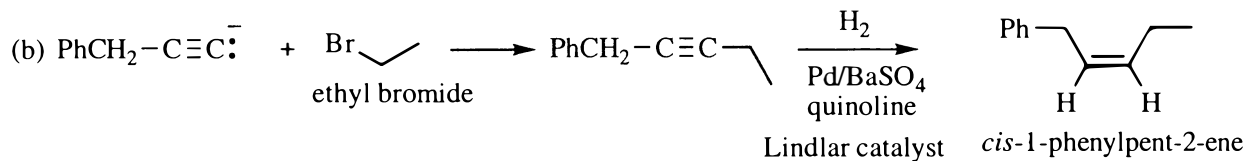
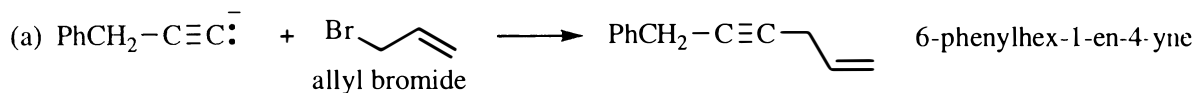
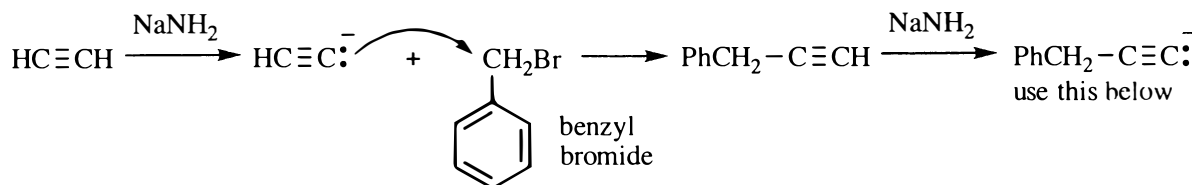
2 carboxylic acids $\Rightarrow$ 1 alkyne



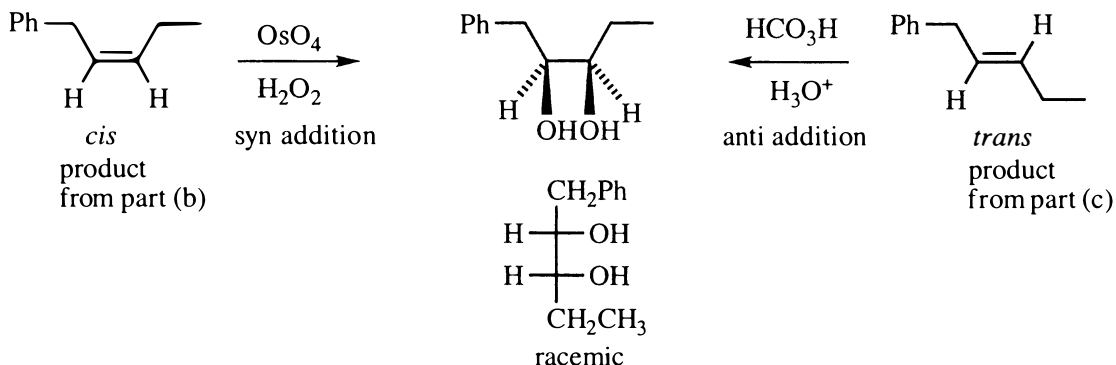
Whether the alkene is cis or trans cannot be determined from these results.

$$\text{ozonolysis} \Rightarrow \text{CH}_3(\text{CH}_2)_4\overset{\text{O}}{\parallel}\text{C}-\text{H} \quad \underbrace{\text{CH}_3-\overset{\text{O}}{\parallel}\text{C}-\text{CH}_2}_{\text{from alkene}} - \underbrace{\overset{\text{O}}{\parallel}\text{C}-\text{OH} \quad \text{HO}-\overset{\text{O}}{\parallel}\text{C}-\text{H}}_{\text{from alkyne}}$$


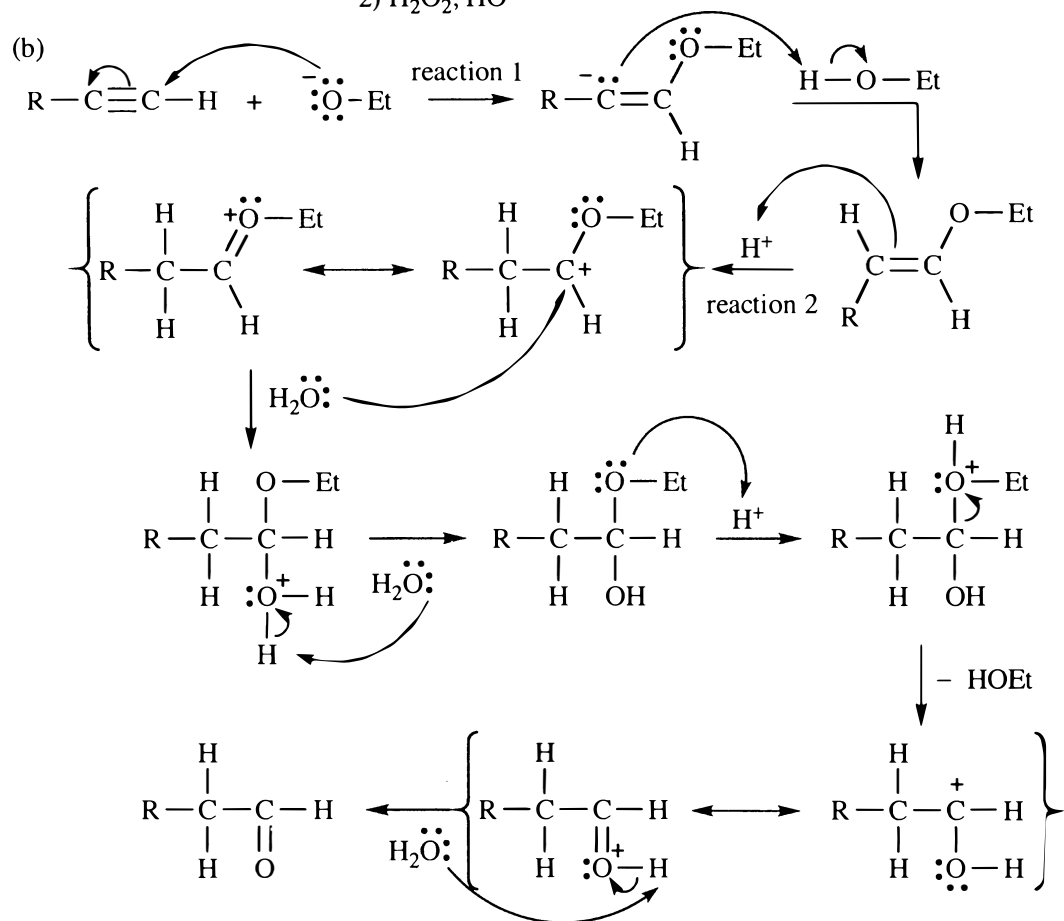
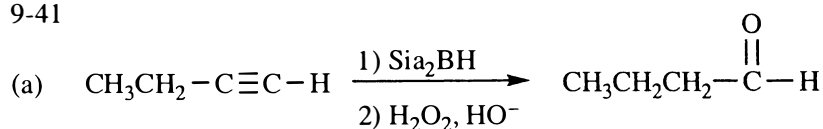
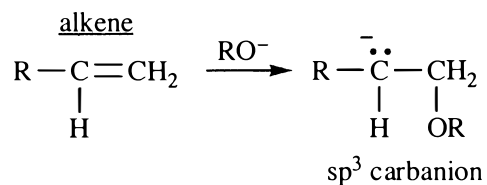
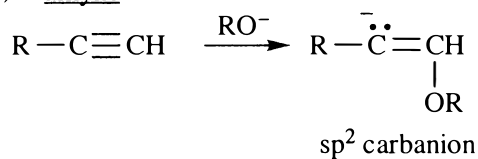
9-40 All four syntheses in this problem begin with the same reaction of benzyl bromide with acetylide ion:



(d) The diol with the two OH groups on the same side in the Fischer projection is the equivalent of a meso structure, although this one is not meso because the top and bottom group are different. Still, it gives a clue as to its synthesis. The "meso" diol can be formed by either a syn addition to a cis double bond, or by an anti addition to a trans double bond. We saw the same thing in the solution to 9-37 (j).



9-41

(c) alkyne

The closer that electrons are to the nucleus, the more stable. An s orbital is closer to a nucleus than a p orbital is, as p orbitals are elongated away from the nucleus. An sp^2 carbanion is more stable than an sp^3 carbanion because the sp^2 carbanion has 33% s character and the electron pair is closer to the positive nucleus than in an sp^3 carbanion which is only 25% s character. The sp^2 carbanion is easier to form because of its relative stability.

9-42 Diols are made by two reactions from Chapter 8 and revisited in 9-41 (d): either syn-dihydroxylation with OsO_4 , or anti-dihydroxylation via an epoxide using a peroxyacid and water. As this problem says to use inorganic reagents, the solution shown here will use OsO_4 .

Recall the stereochemical requirements of syn addition as outlined in this Solutions Manual, p. 171, Problem 8-35:

cis-alkene + **syn** addition $\rightarrow$ meso

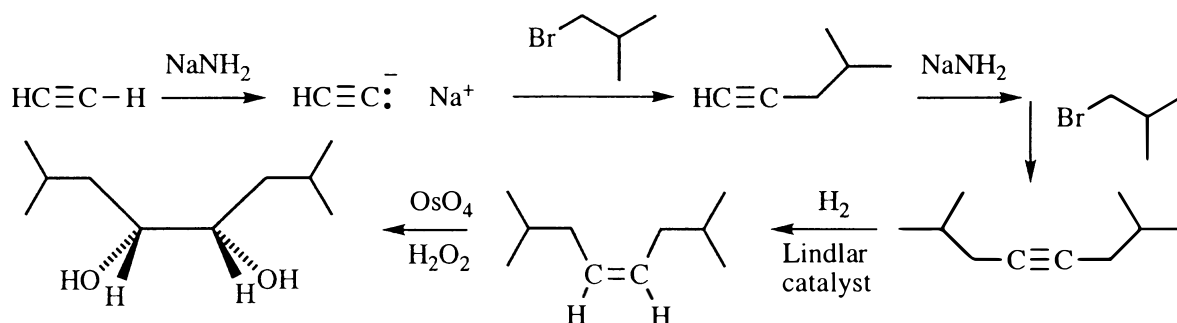
cis-alkene + **anti** addition $\rightarrow$ racemic ($\pm$)

trans-alkene + **syn** addition $\rightarrow$ racemic ($\pm$)

trans-alkene + **anti** addition $\rightarrow$ meso

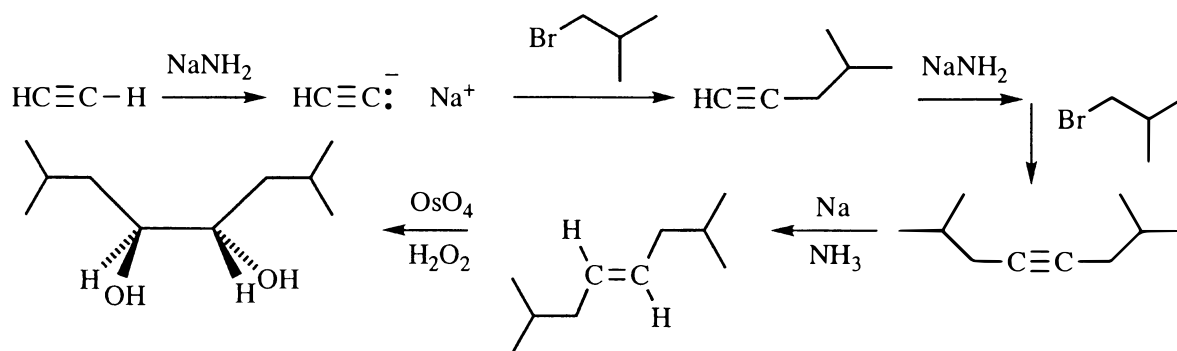
Part (a) asks for the synthesis of the meso isomer, so syn addition will have to occur on the *cis*-alkene. Part (b) will require syn addition to the *trans*-alkene to give the ($\pm$) product.

(a)



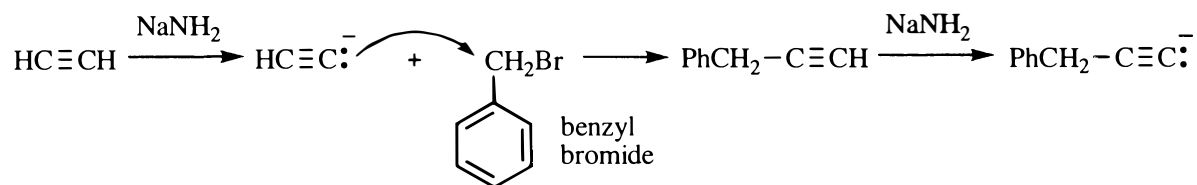
alkene must be *cis* to produce the meso product from syn addition, so reduction is done with Lindlar catalyst to produce the *cis* alkene

(b)

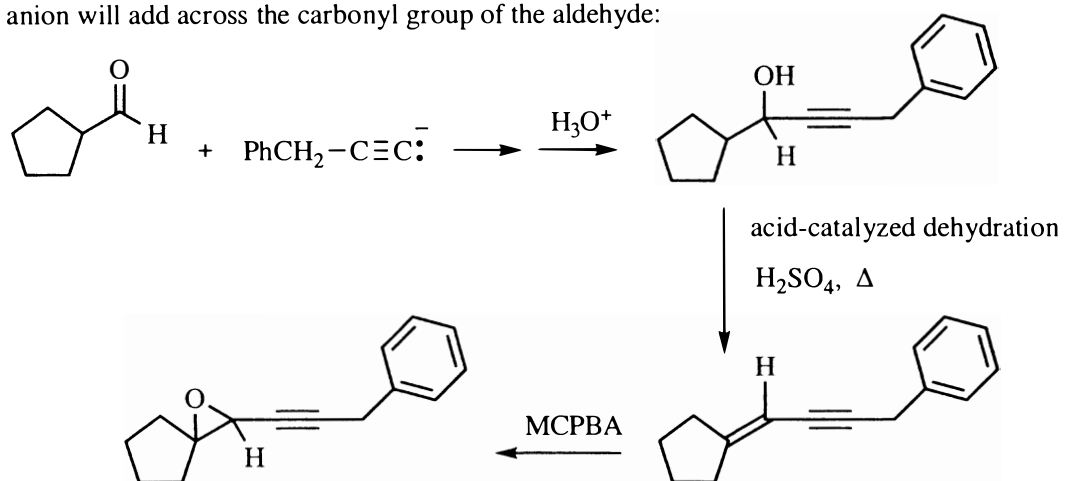


alkene must be *trans* to produce the ($\pm$) product from syn addition, so reduction is done with Na/NH_3

9-43 This synthesis begins the same as the solution to problem 9-40:



The anion will add across the carbonyl group of the aldehyde:



CHAPTER 10—STRUCTURE AND SYNTHESIS OF ALCOHOLS

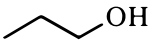
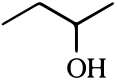
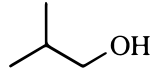
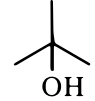
10-1 Please see the note on p. 136 of this Solutions Manual regarding placement of position numbers.

- | | |
|--|---|
| (a) 2-phenylpropan-2-ol | (d) <i>trans</i> -2-methylcyclohexan-1-ol ("1" is optional) |
| (b) 5-bromoheptan-2-ol | (e) (<i>E</i>)-2-chloro-3-methylpent-2-en-1-ol |
| (c) 4-methylcyclohex-3-en-1-ol ("1" is optional) | (f) (2 <i>R</i> ,3 <i>S</i>)-2-bromohexan-3-ol |

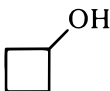
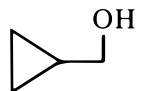
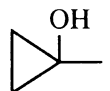
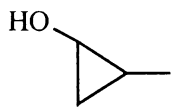
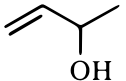
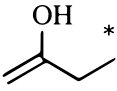
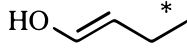
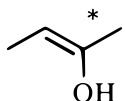
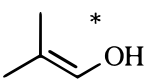
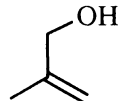
10-2 IUPAC name first, then common name.

- | | |
|--|---|
| (a) cyclopropanol; cyclopropyl alcohol | (c) 1-cyclobutylpropan-2-ol; no common name |
| (b) 2-methylpropan-2-ol; <i>t</i> -butyl alcohol | (d) 3-methylbutan-1-ol; isopentyl alcohol
(also isoamyl alcohol) |

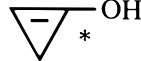
10-3 Only constitutional isomers are requested, not stereoisomers, and only structures with an alcohol group.

- (a) C_3H_8O  propan-1-ol  propan-2-ol
- (b) $C_4H_{10}O$  butan-1-ol  butan-2-ol  2-methylpropan-1-ol  2-methylpropan-2-ol

(c) C_4H_8O has one element of unsaturation, either a double bond or a ring.

- | | | | |
|---|---|---|---|
|  |  |  |  |
| cyclobutanol | cyclopropylmethanol | 1-methylcyclopropanol | 2-methylcyclopropanol
<i>cis</i> or <i>trans</i> |
|  |  |  |  |
| but-3-en-1-ol | but-3-en-2-ol | but-1-en-2-ol | but-1-en-1-ol (<i>E</i> or <i>Z</i>) |
|  |  |  |  |
| but-2-en-1-ol
(<i>E</i> or <i>Z</i>) | but-2-en-2-ol
(<i>E</i> or <i>Z</i>) | 2-methylprop-1-en-1-ol | 2-methylprop-2-en-1-ol |

(d) C_3H_4O has two elements of unsaturation, so each structure must have either a triple bond, or two double bonds, or a three-membered ring and a double bond. All structures must contain an OH. (In the name, the "e" is dropped from "yne" because it follows by a vowel in "ol".)

- | | | | | |
|----------------------------------|--------------------------------|--------------------------|--|---|
| $HO-\overset{*}{C}\equiv C-CH_3$ | $HC\equiv C-\overset{*}{CH_2}$ | $H_2C=C=\overset{*}{CH}$ |  |  |
| prop-1-yn-1-ol | prop-2-yn-1-ol | propa-1,2-dien-1-ol | cycloprop-1-en-1-ol | cycloprop-2-en-1-ol |

*These compounds with the OH bonded directly to the carbon-carbon double bond are called "enols" or "vinyl alcohols." The structure with OH on a carbon-carbon triple bond is called an ynol. These are unstable, although the structures are legitimate.

- 10-4 (a) 8,8-dimethylnonane-2,7-diol
 (b) octane-1,8-diol
 (c) *cis*-cyclohex-2-ene-1,4-diol
 (d) 3-cyclopentylheptane-2,4-diol
 (e) *trans*-cyclobutane-1,3-diol

10-5 There are four structural features to consider when determining solubility in water: 1) molecules with fewer carbons will be more soluble in water (assuming other things being equal); 2) branched or otherwise compact structures are more soluble than linear structures; 3) more hydrogen-bonding groups will increase solubility; 4) an ionic form of a compound will be more soluble in water than the nonionic form.

- (a) Cyclohexanol is more soluble because its alkyl group is more compact than in 1-hexanol.
 (b) 4-Methylphenol is more soluble because its hydrocarbon portion is more compact than in 1-heptanol, and phenols form particularly strong hydrogen bonds with water.
 (c) 3-Ethylhexan-3-ol is more soluble because its alkyl portion is more spherical than in octan-2-ol.
 (d) Cyclooctane-1,4-diol is more soluble because it has two OH groups which can hydrogen bond with water, whereas hexan-2-ol has only one OH group. (The ratio of carbons to OH is 4 to 1 in the former compound and 6 to 1 in the latter; the smaller this ratio, the more soluble.)
 (e) These are enantiomers and will have identical solubility.

10-6 Dimethylamine molecules can hydrogen bond among themselves so it takes more energy (higher temperature) to separate them from each other. Trimethylamine has no N-H and cannot hydrogen bond, so it takes less energy to separate these molecules from each other, despite its higher molecular weight.

10-7 See Appendix 2 at the back of this Solutions Manual for a review of acidity and basicity.

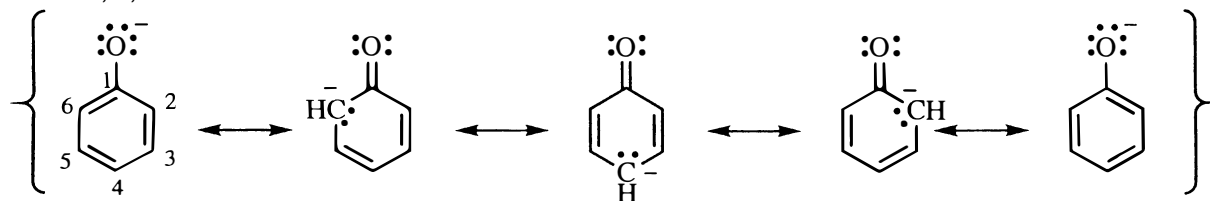
- (a) Methanol is more acidic than *t*-butyl alcohol. The greater the substitution, the lower the acidity.
 (b) 2-Chloropropan-1-ol is more acidic because the electron-withdrawing chlorine atom is closer to the OH group than in 3-chloropropan-1-ol.
 (c) 2,2-Dichloroethanol is more acidic because two electron-withdrawing chlorine atoms increase acidity more than just the one chlorine in 2-chloroethanol.
 (d) 2,2-Difluoropropan-1-ol is more acidic because fluorine is more electronegative than chlorine; the stronger the electron-withdrawing group, the more acidic the alcohol.

10-8

most acidic								least acidic				
sulfuric acid	>>	2-chloroethanol	>	water	>	ethanol	>	<i>t</i> -butyl alcohol	>	ammonia	>	hexane
H ₂ SO ₄		ClCH ₂ CH ₂ OH		H ₂ O		CH ₃ CH ₂ OH		(CH ₃) ₃ COH		NH ₃		C ₆ H ₁₄

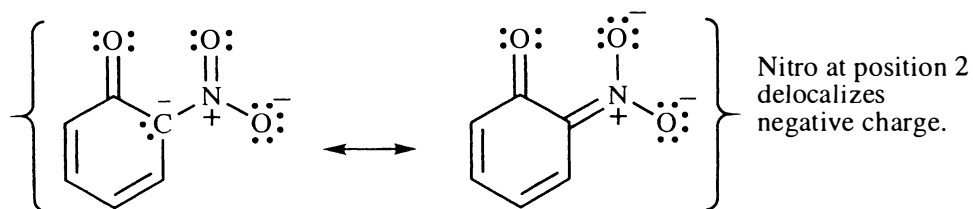
Sulfuric acid is one of the strongest acids known. On the other extreme, alkanes like hexane are the least acidic compounds. The N-H bond in ammonia is less acidic than any O-H bond. Among the four compounds with O-H bonds, the tertiary alcohols are the least acidic. Water is more acidic than most alcohols including ethanol. However, if a strong electron-withdrawing substituent like chlorine is near the alcohol group, the acidity increases enough so that it is more acidic than water. (Determining exactly where water appears in this list is the most difficult part.)

10-9 Resonance forms of phenoxide anion show the negative charge delocalized onto the ring only at carbons 2, 4, and 6:

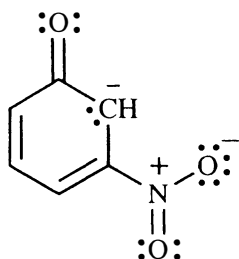


10-9 continued

Nitro group at position 2

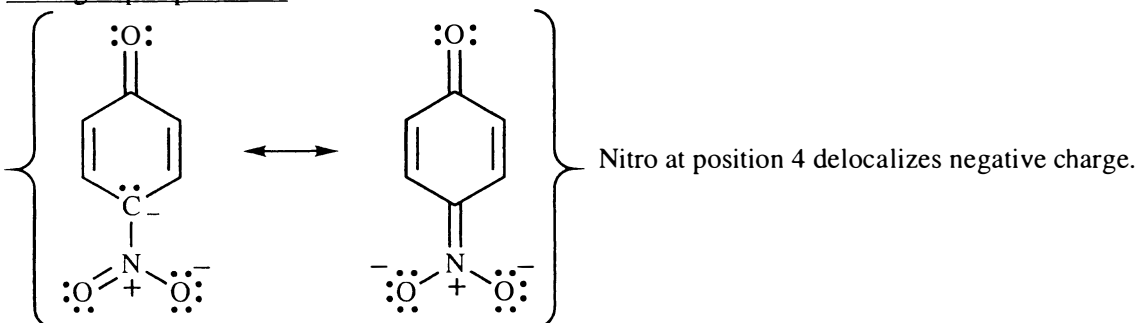


Nitro group at position 3



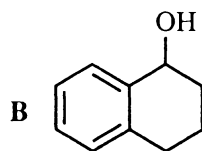
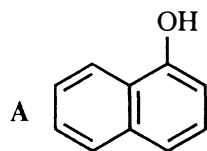
Nitro at position 3 cannot delocalize negative charge at position 2 or 4—no resonance stabilization.

Nitro group at position 4



Only when the nitro group is at one of the negative carbons will the nitro have a stabilizing effect (via resonance). Thus, 2-nitrophenol and 4-nitrophenol are substantially more acidic than phenol itself, but 3-nitrophenol is only slightly more acidic than phenol (due to the inductive effect).

10-10

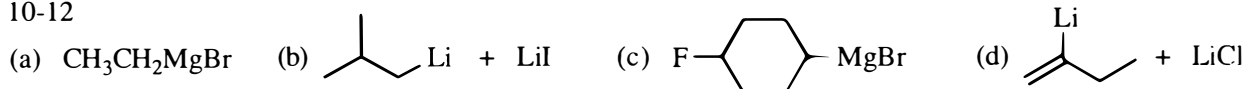


(a) Structure **A** is a phenol because the OH is bonded to a benzene ring. As a phenol, it will be acidic enough to react with sodium hydroxide to generate a phenoxide ion that will be fairly soluble in water. Structure **B** is a 2° benzylic alcohol, not a phenol, not acidic enough to react with NaOH.

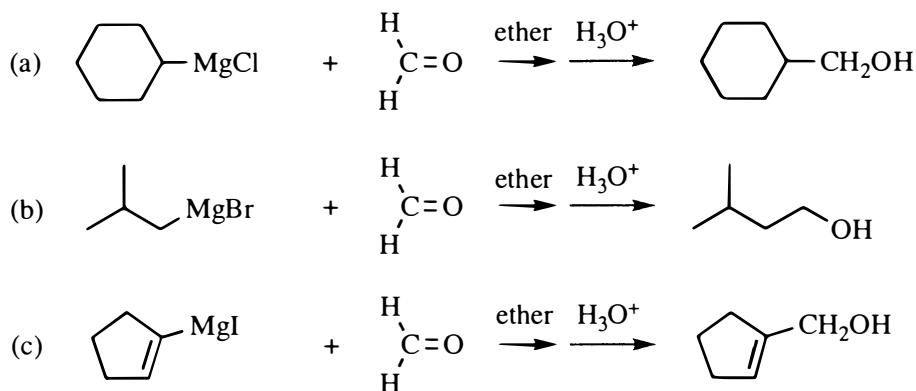
(b) Both of these organic compounds will be soluble in an organic solvent like dichloromethane. Shaking this organic solution with aqueous sodium hydroxide will ionize the phenol **A**, making it more polar and water soluble; it will be extracted from the organic layer into the water layer, while the alcohol will remain in the organic solvent. Separating these immiscible solvents will separate the original compounds. The alcohol can be retrieved by evaporating the organic solvent. The phenol can be isolated by acidifying the basic aqueous solution and filtering if the phenol is a solid, or separating the layers if the phenol is a liquid.

10-11 The Grignard reaction needs a solvent containing an ether functional group: (b), (f), (g), and (h) are possible solvents. Dimethyl ether, (b), is a gas at room temperature, however, so it would have to be liquefied at low temperature for it to be a useful solvent.

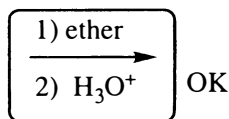
10-12



10-13 Any of three halides—chloride, bromide, iodide, but not fluoride—can be used. Ether is the typical solvent for Grignard reactions.

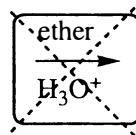


Note: the alternative arrow symbolism could also be used, where the two steps are numbered around one arrow:



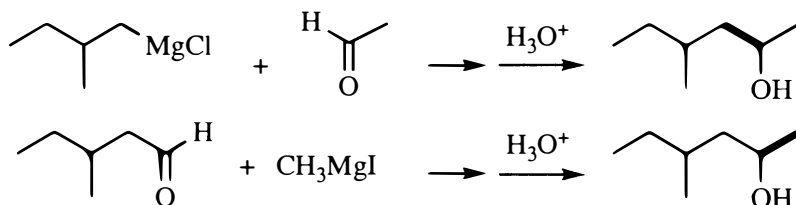
NO! Me BAD!

This means that water is present with ether during the Grignard reaction.



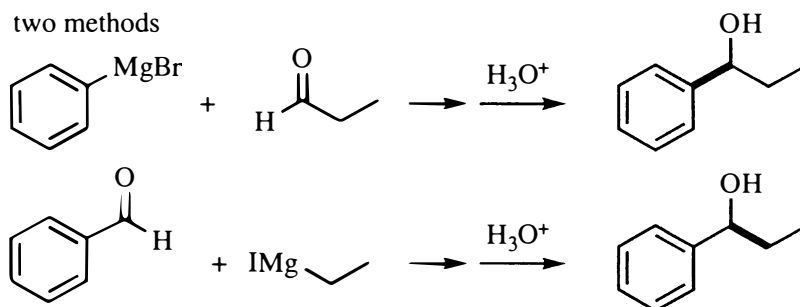
10-14 Any of three halides—chloride, bromide, iodide, but not fluoride—can be used. Grignard reactions are always performed in ether solvent; ether is not shown here.

(a) two methods

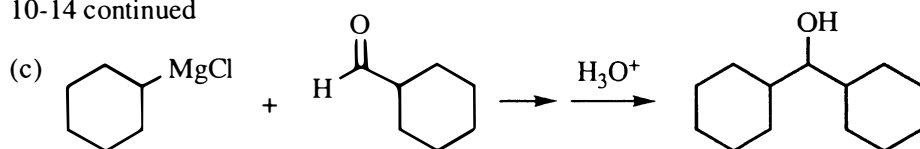


Where two methods can be used to form the target compound, the newly formed bond is shown in bold.

(b) two methods

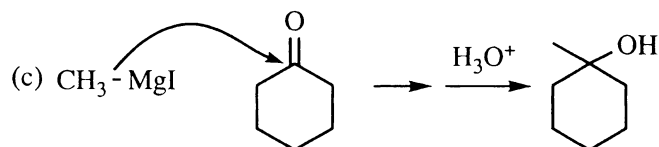
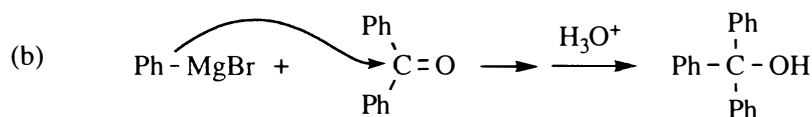
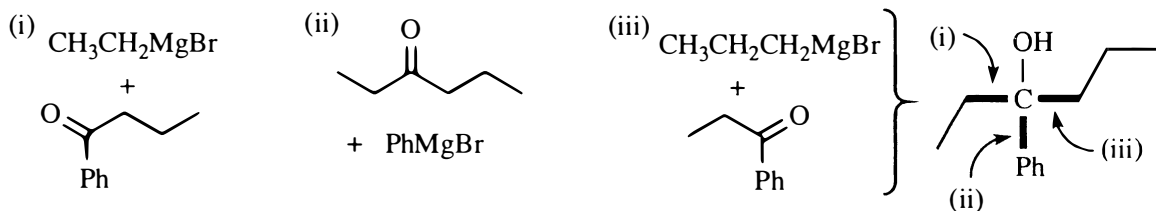


10-14 continued

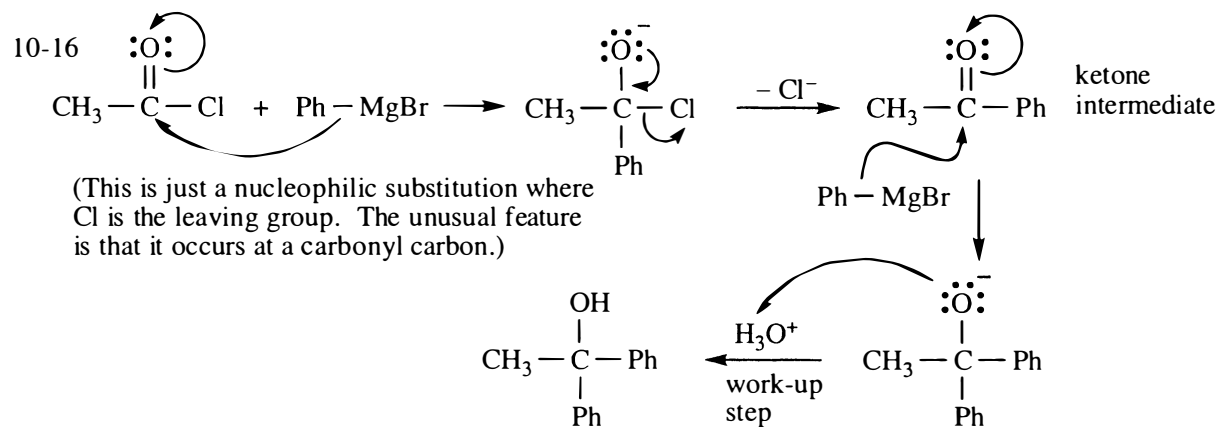
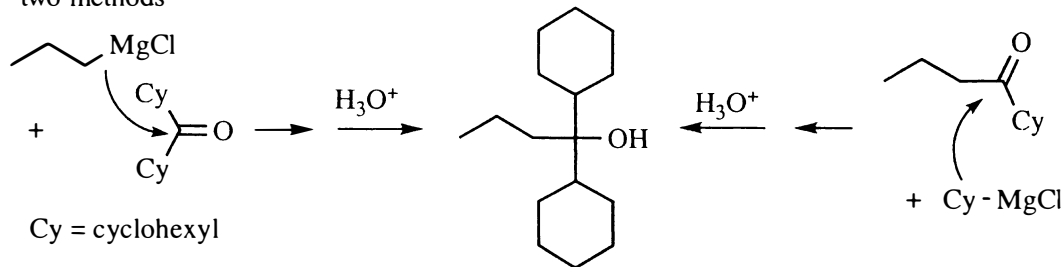


10-15 Grignard reactions are always performed in ether. Here, the ether is not shown.

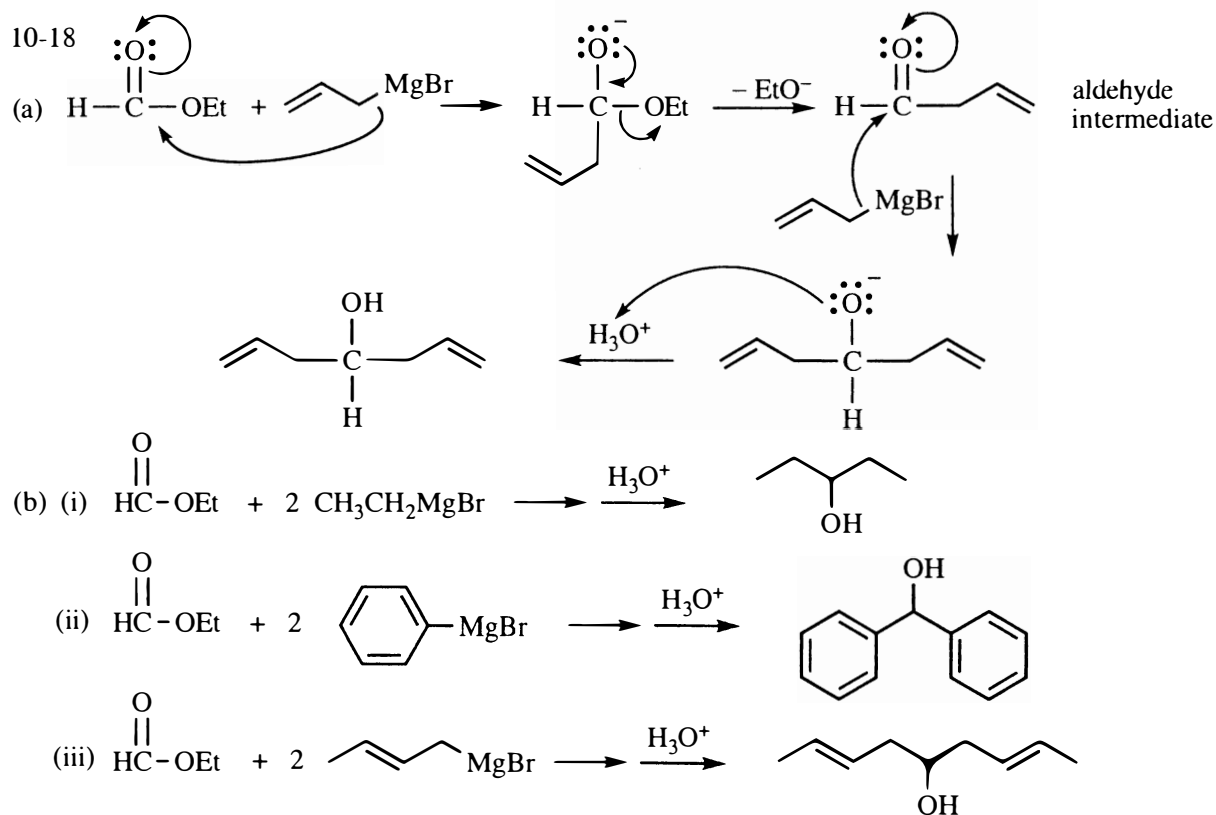
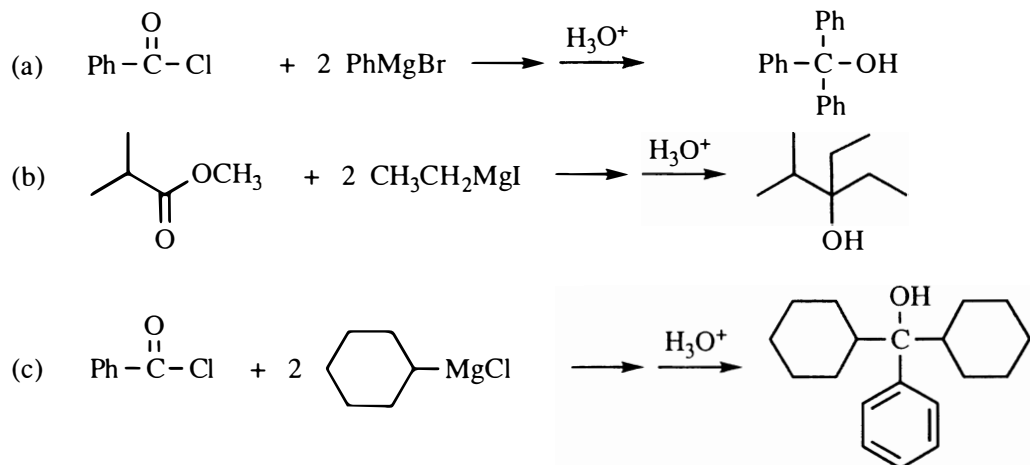
(a) Any of the three bonds shown in bold can be formed by adding a Grignard reagent across a ketone.



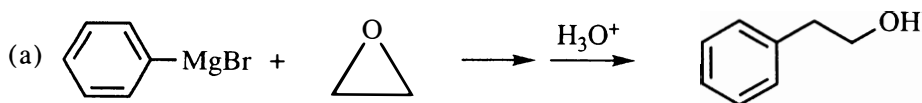
(d) two methods



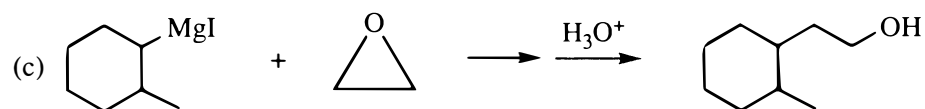
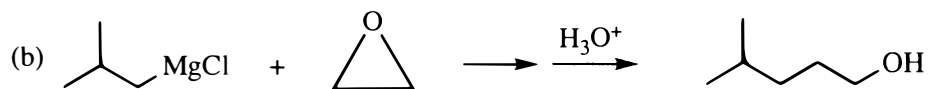
10-17 Acid chlorides or esters will work as starting materials in these reactions. The typical solvent for Grignard reactions is ether; it is not shown here.



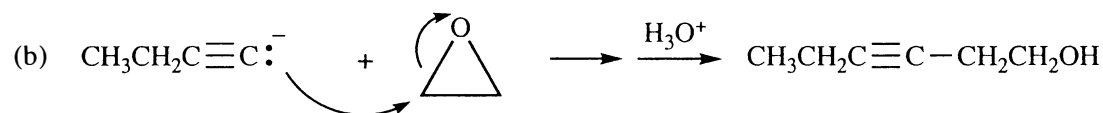
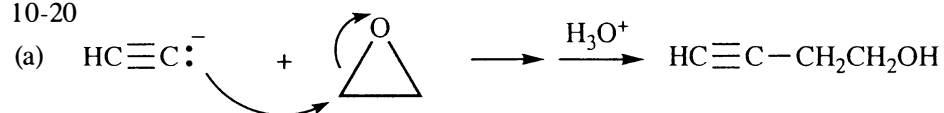
10-19 Ether is the typical solvent in Grignard reactions.



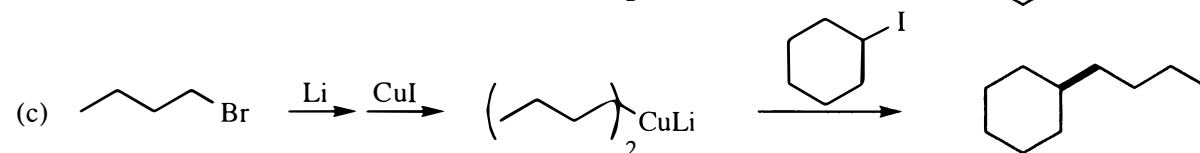
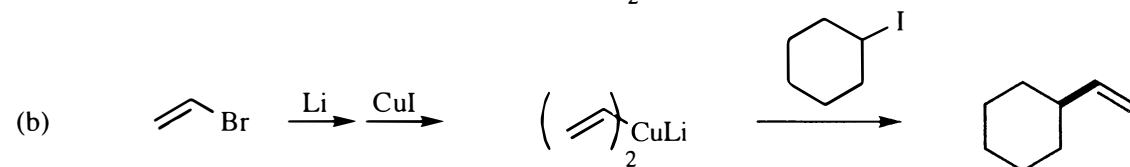
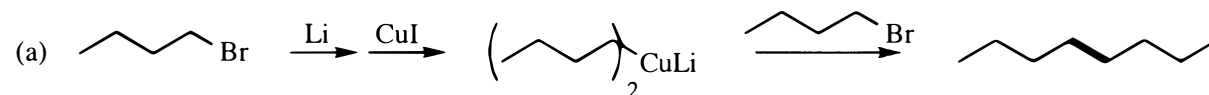
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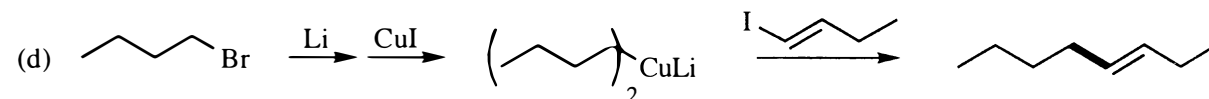
10-20



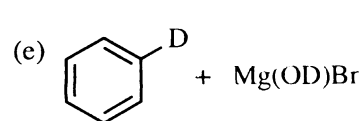
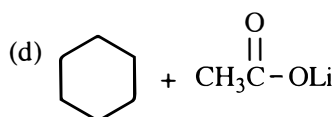
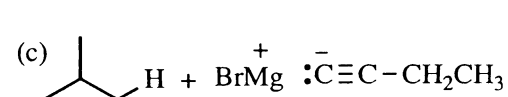
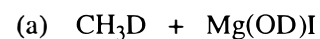
10-21 There are more than one synthetic route to each structure; the ones shown here are representative. The new bonds formed are shown here in bold. Your answers may be different and still be correct.



Alternatively, coupling lithium dicyclohexylcuprate with 1-bromobutane would also work. As this mechanism is not a typical S_N2 , it is not as susceptible to steric hindrance like acetylide ion substitution or a similar S_N2 reaction.



10-22 These reactions are acid-base reactions in which an acidic proton (or deuteron) is transferred to a basic carbon in either a Grignard reagent or an alkyl lithium.



10-23 Grignard reagents are incompatible with acidic hydrogens and with electrophilic, polarized multiple bonds like C=O, NO₂, etc.

(a) As Grignard reagent is formed, it would instantaneously be protonated by the N—H present in other molecules of the same substance.

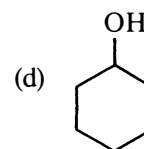
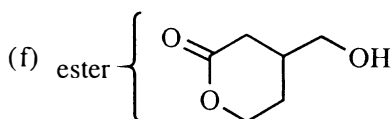
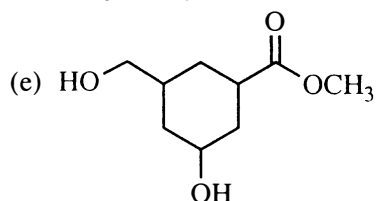
(b) As Grignard reagent is formed, it would immediately attack the ester functional group present in other molecules of the same substance.

(c) Care must be taken in how reagents are written above and below arrows. If reagents are numbered "1. ... 2. ... etc.", it means they are added in separate steps, the same as writing reagents over separate arrows. If reagents written around an arrow are not numbered, it means they are added all at once in the same mixture. In this problem, the ketone is added in the presence of aqueous acid. The acid will immediately protonate and destroy the Grignard reagent before reaction with the ketone can occur.

(d) The ethyl Grignard reagent will be immediately protonated and consumed by the OH. This reaction *could* be made to work, however, by adding two equivalents of ethyl Grignard reagent—the first to consume the OH proton, the second to add across the ketone. Aqueous acid will then protonate both oxygens.

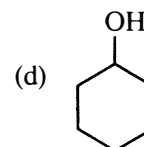
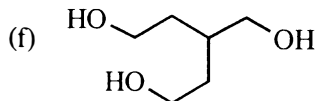
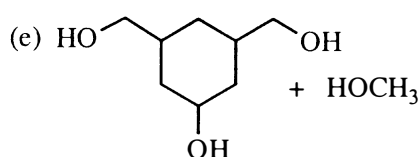
10-24 Sodium borohydride does not reduce esters.

(a) CH₃(CH₂)₈CH₂OH (b) no reaction (c) no reaction (PhCOO[−] before acid work-up)

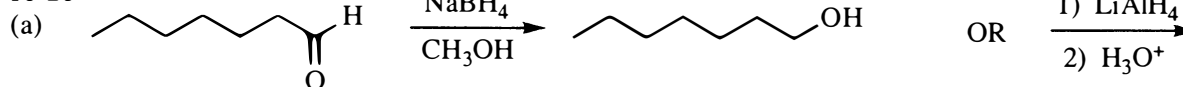


10-25 Lithium aluminum hydride reduces esters as well as other carbonyl groups.

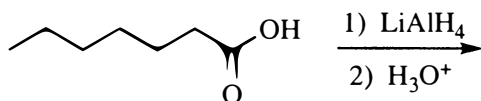
(a) CH₃(CH₂)₈CH₂OH (b) CH₃CH₂CH₂OH + HOCH₃ (c) PhCH₂OH



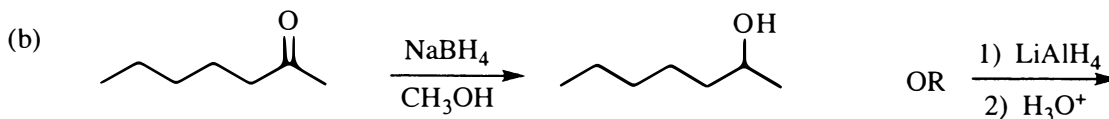
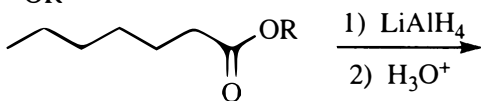
10-26



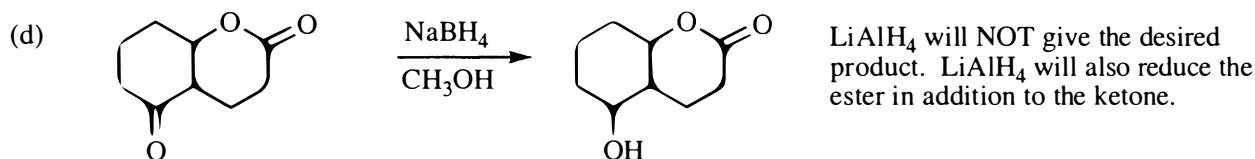
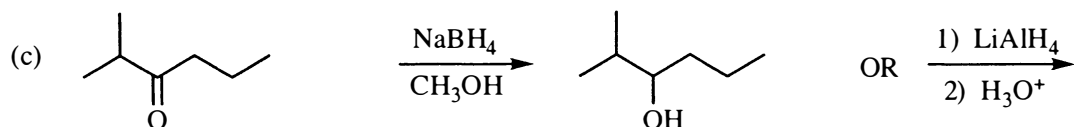
OR



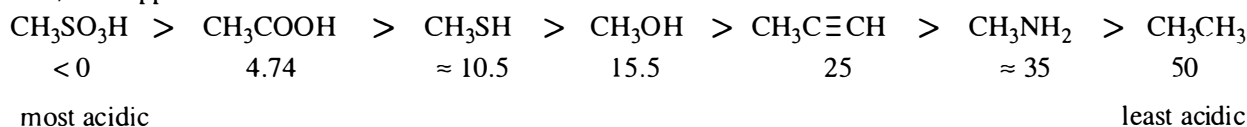
OR



10-26 continued

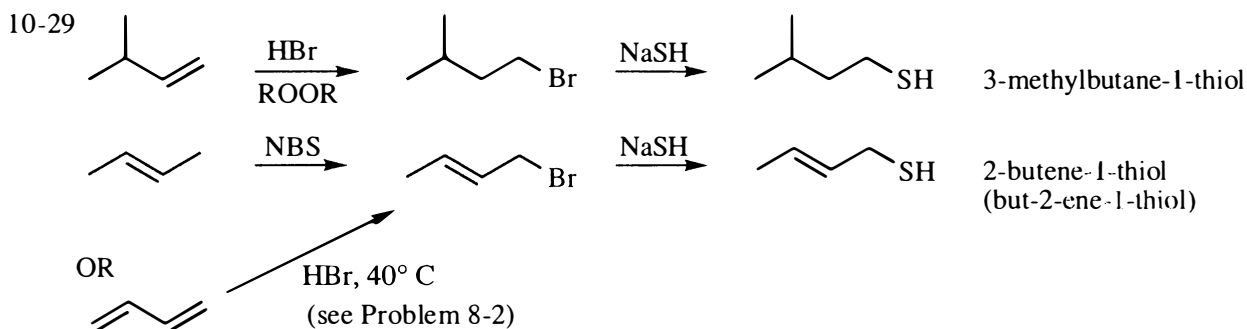


10-27 Approximate pKa values are shown below each compound. Refer to text Tables 1-5, 9-2, and 10-3, and Appendix 5 at the back of the text.



10-28

- (a) 4-methylpentane-2-thiol
 (b) (Z)-2,3-dimethylpent-2-ene-1-thiol ("1" is optional)
 (c) cyclohex-2-ene-1-thiol ("1" is optional)



10-30 Please refer to solution 1-20, page 12 of this Solutions Manual.

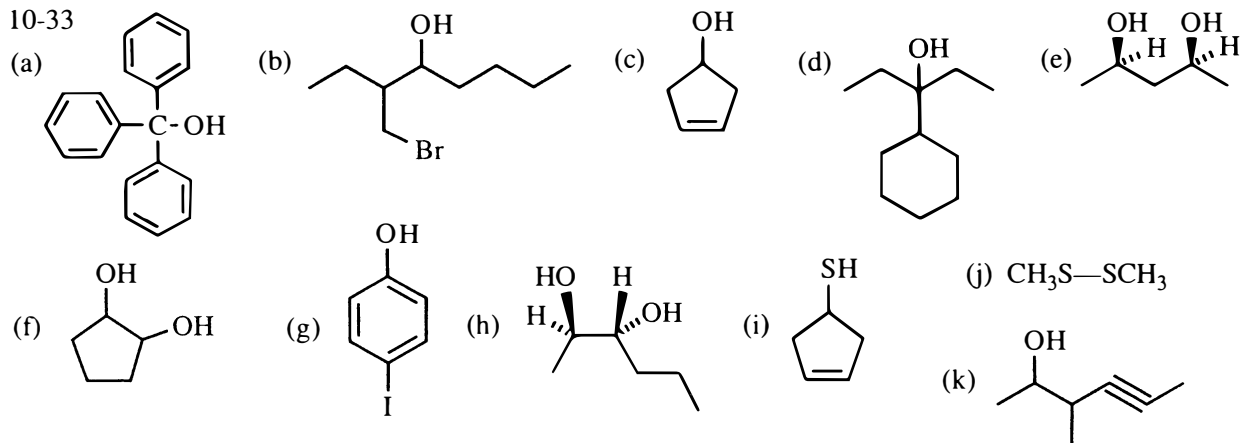
10-31

- (a) 5-methyl-4-*n*-propylheptan-2-ol; 2°
 (b) 4-(1-bromoethyl)heptan-3-ol; 2°
 (c) (*E*)-4,5-dimethylhex-3-en-1-ol; 1°
 (d) 3-bromocyclohex-3-en-1-ol; 2° ("1" is optional)
 (e) *cis*-4-chlorocyclohex-2-en-1-ol; 2° ("1" is optional)
 (f) 6-chloro-3-phenyloctan-3-ol; 3°
 (g) (1-cyclopentenyl)methanol; 1°

10-32

- (a) 4-chloro-1-phenylhexane-1,5-diol
 (b) *trans*-cyclohexane-1,2-diol
 (c) 3-nitrophenol
 (d) 4-bromo-2-chlorophenol

10-33



10-34

- (a) Hexan-1-ol will boil at a higher temperature as it is less branched than 3,3-dimethylbutan-1-ol.
 (b) Hexan-2-ol will boil at a higher temperature because its molecules hydrogen bond with each other, whereas molecules of hexan-2-one have no intermolecular hydrogen bonding.
 (c) Hexane-1,5-diol will boil at a higher temperature as it has two OH groups for hydrogen bonding. Hexan-2-ol has only one group for hydrogen bonding.
 (d) Hexan-2-ol will boil at a higher temperature because it has a higher molecular weight than pentan-2-ol. All other structural features of the two molecules are the same, so they should have the same intermolecular forces.

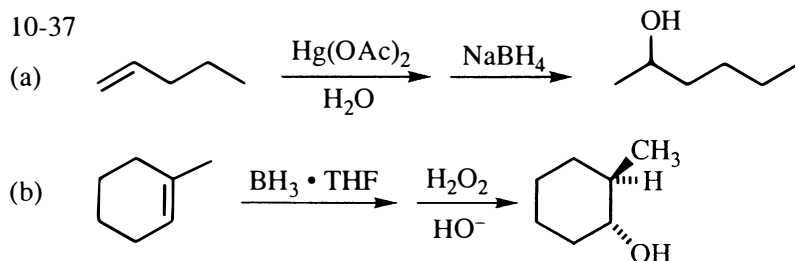
10-35

- (a) 3-Chlorophenol is more acidic than cyclopentanol. In general, phenols are many orders of magnitude more acidic than alcohols.
 (b) 2-Chlorocyclohexanol is slightly more acidic than cyclohexanol; the proximity of the electronegative chlorine to the OH increases its acidity.
 (c) Cyclohexanecarboxylic acid is more acidic than cyclohexanol. In general, carboxylic acids are many orders of magnitude more acidic than alcohols.
 (d) 2,2-Dichlorobutan-1-ol is more acidic than butan-1-ol because of the two electron-withdrawing substituents near the acidic functional group.

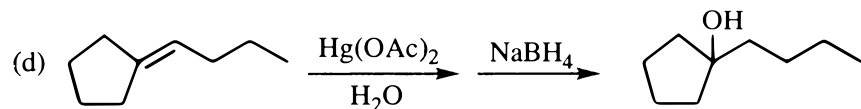
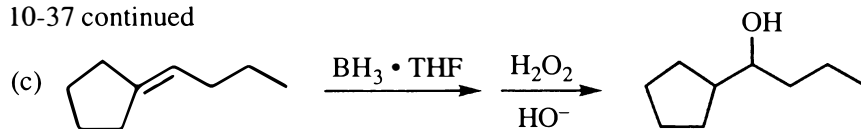
10-36

- (a) Propan-2-ol is the most soluble in water as it has the fewest carbons and the most branching.
 (b) Cyclohexane-1,2-diol is the most soluble as it has two OH groups for hydrogen bonding. Cyclohexanol has only one OH group; chlorocyclohexane cannot hydrogen bond and is the least soluble.
 (c) Cyclohexanol is the most soluble as it can hydrogen bond. Chlorocyclohexane cannot hydrogen bond, and 4-methylcyclohexanol has the added hydrophobic methyl group, decreasing its water solubility.

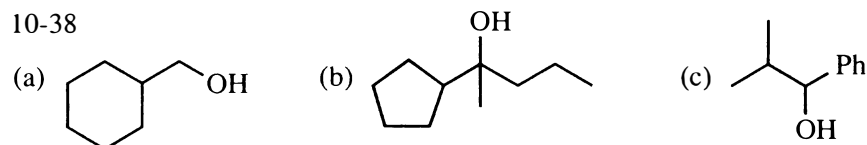
10-37



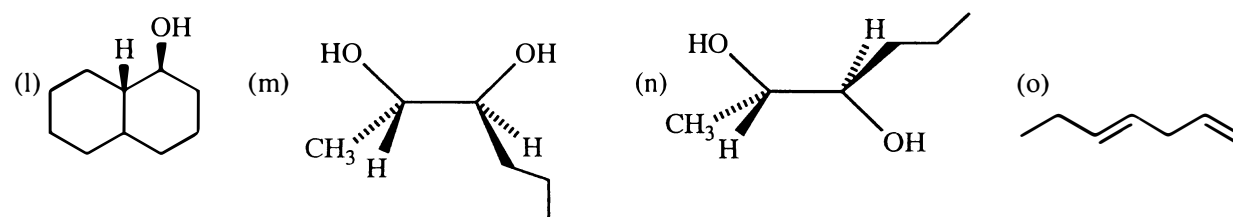
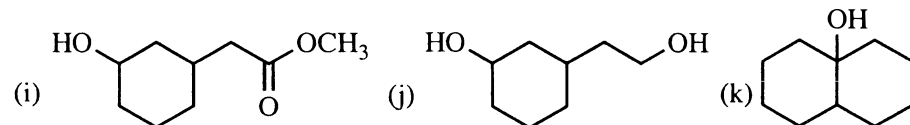
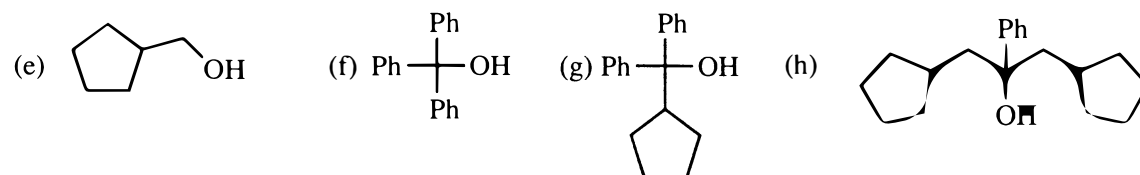
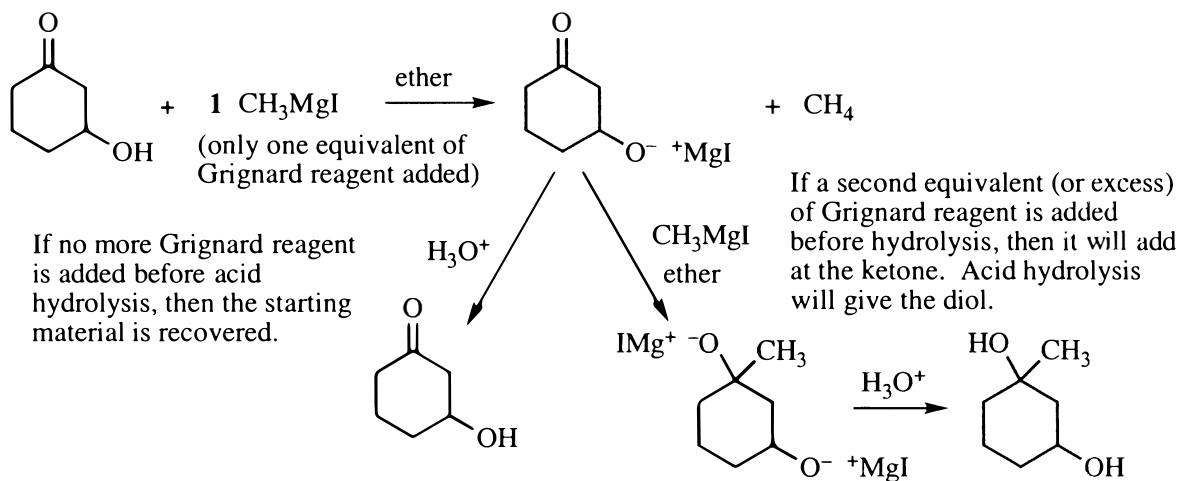
10-37 continued



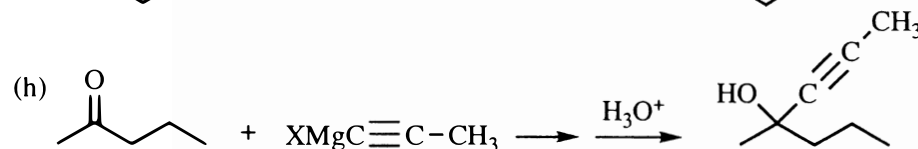
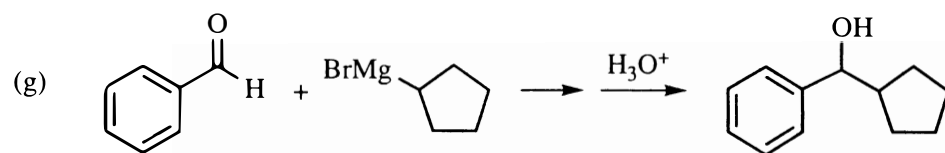
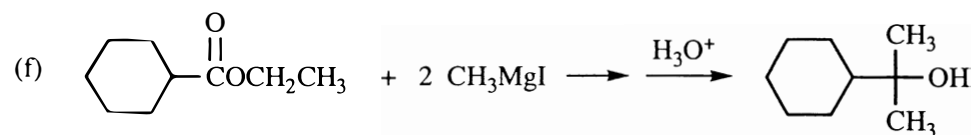
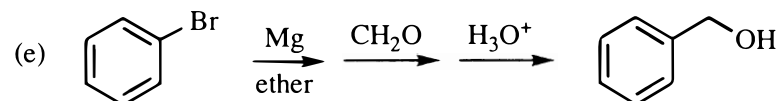
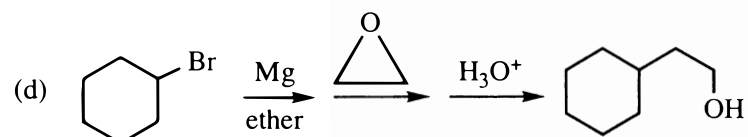
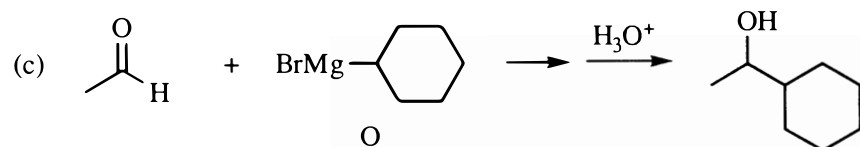
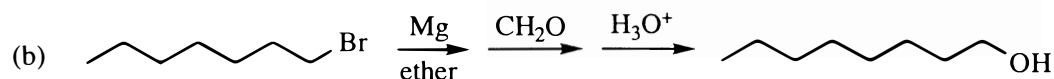
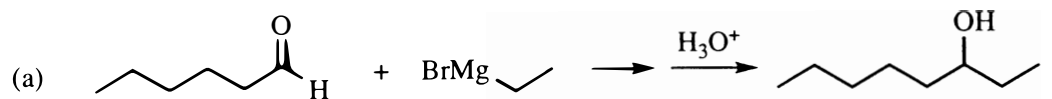
10-38



(d) This problem confuses a lot of people. When a Grignard reagent is added to a compound that has an OH group, the first thing that happens is that the Grignard reacts by removing the H⁺ from the O⁻.



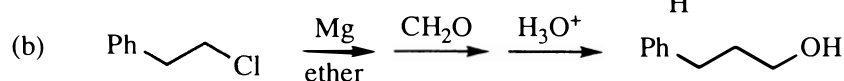
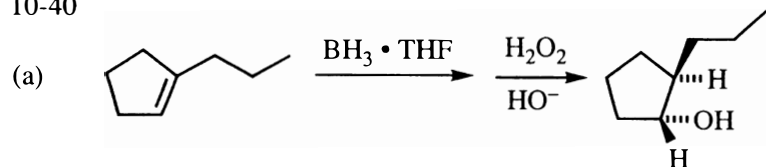
10-39 All Grignard reactions are run in ether solvent. Two arrows are shown indicating that the Grignard reaction is allowed to proceed, and then in a second step, dilute aqueous acid is added.



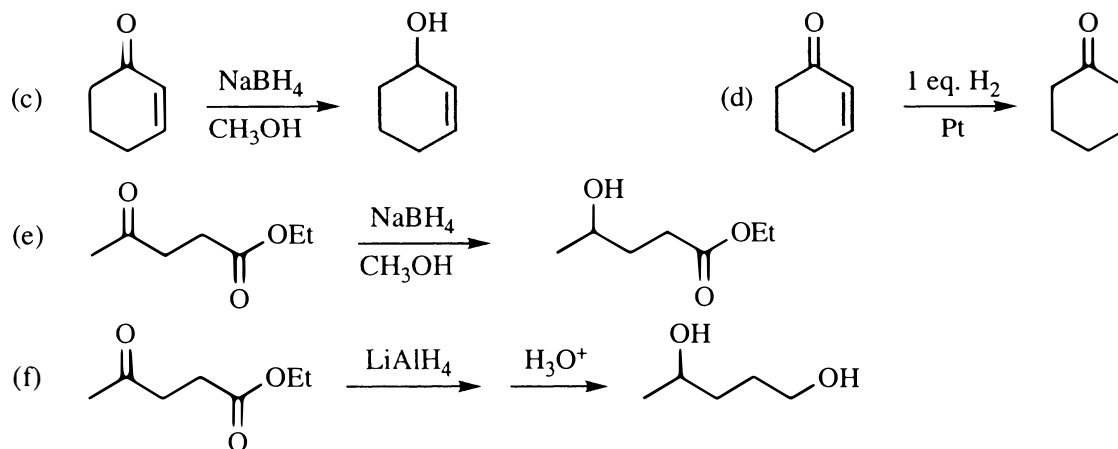
$\text{RMgX} + \text{H}-\text{C}\equiv\text{C}-\text{CH}_3$
any Grignard
reagent where R is
alkyl or alkenyl

Technically, $\text{XMgC}\equiv\text{CCH}_3$ is a Grignard reagent because it is an organometallic compound of magnesium. However, it is not made in the usual fashion; it is made by deprotonating the terminal alkyne as shown.

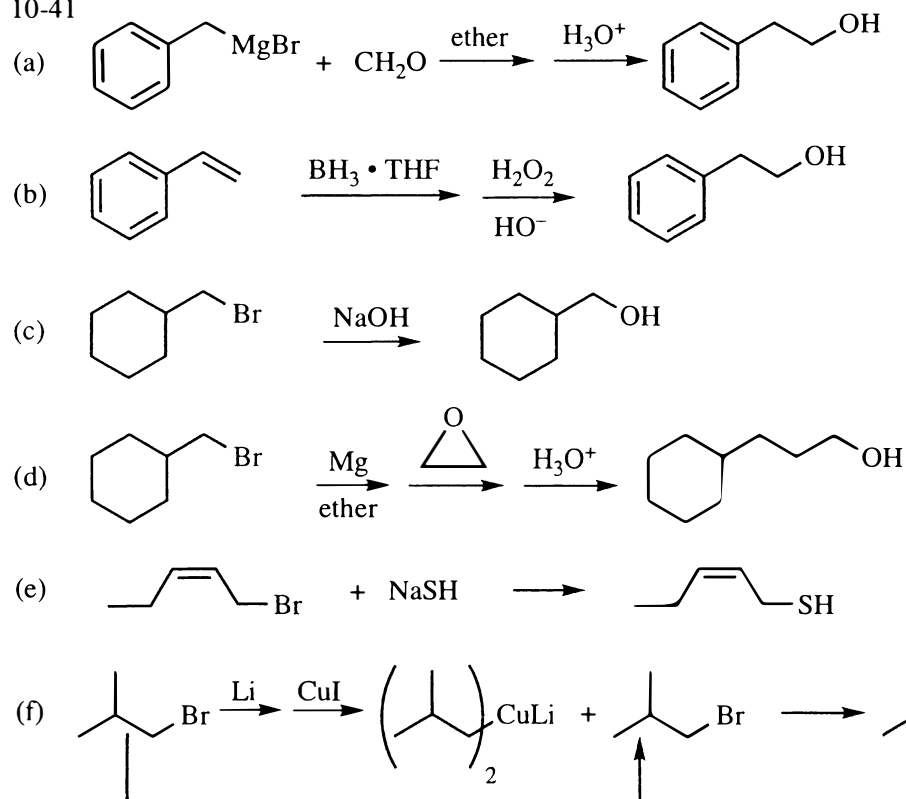
10-40



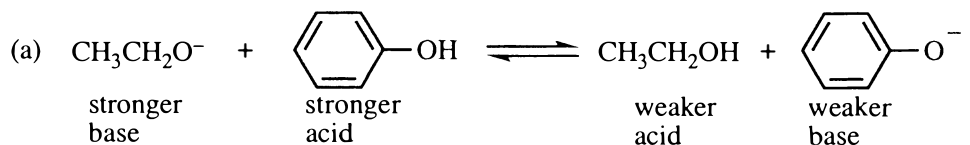
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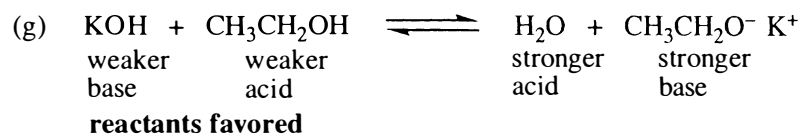
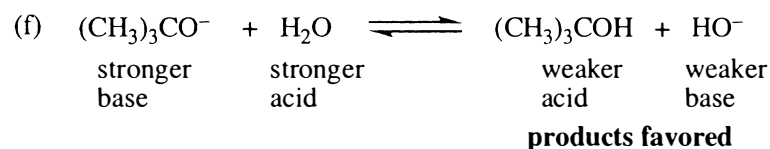
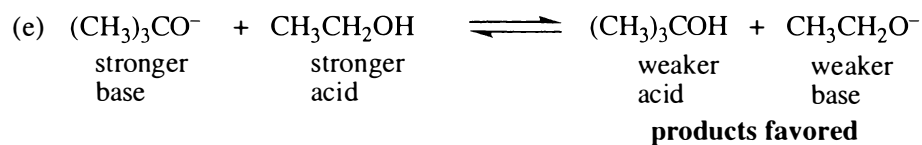
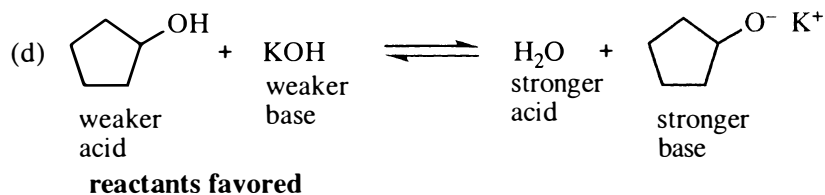
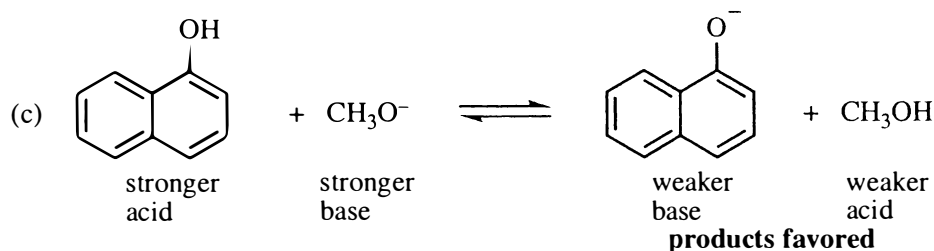
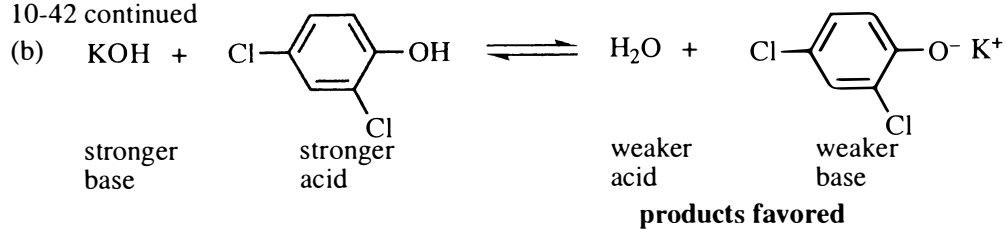
10-41



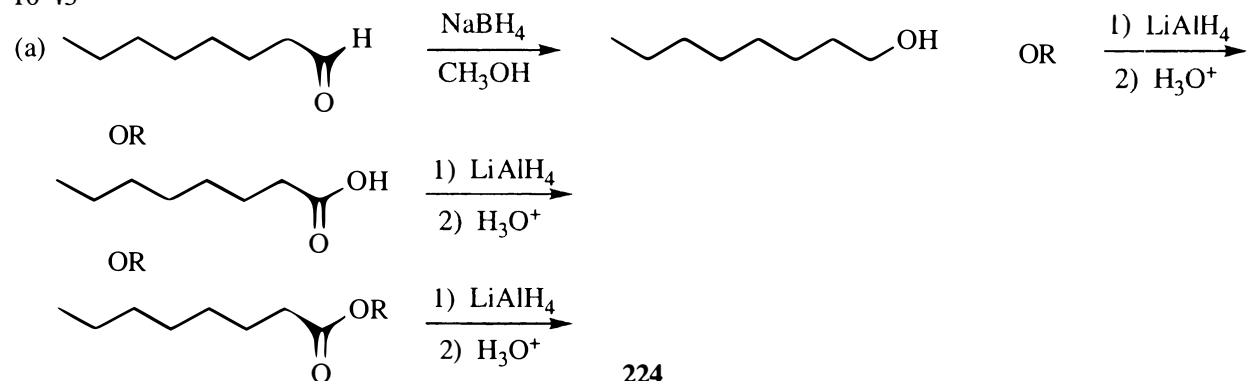
10-42 The position of the equilibrium can be determined by the strength of the acids or the bases. The stronger acid and stronger base will always react to give the weaker acid and base, so the side of the equation with the weaker acid and base will be favored at equilibrium. See Appendix 2 in this Solutions Manual for a review of acidity.



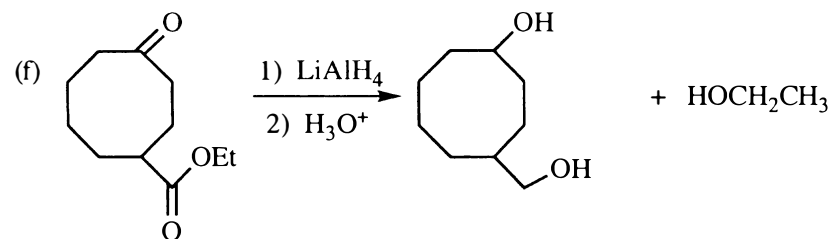
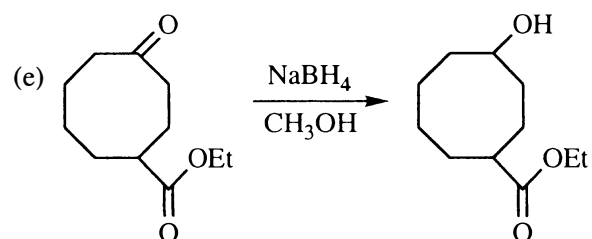
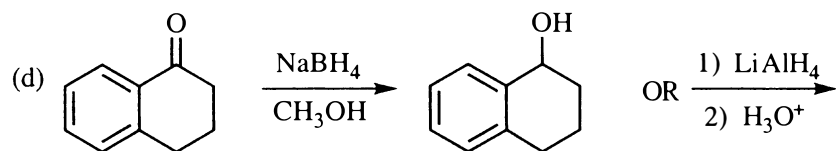
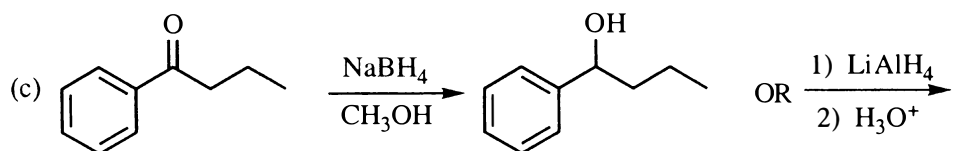
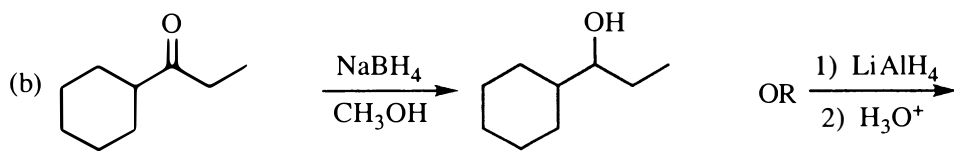
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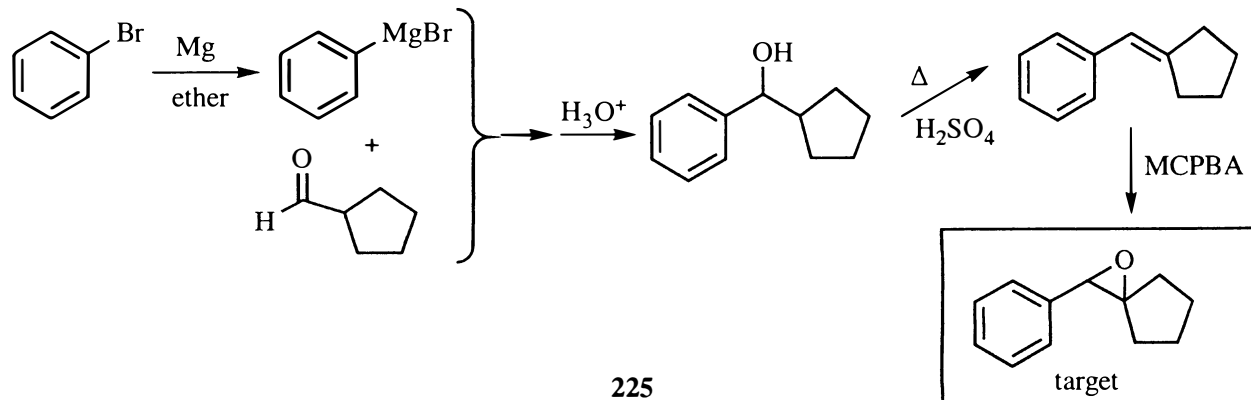
10-43



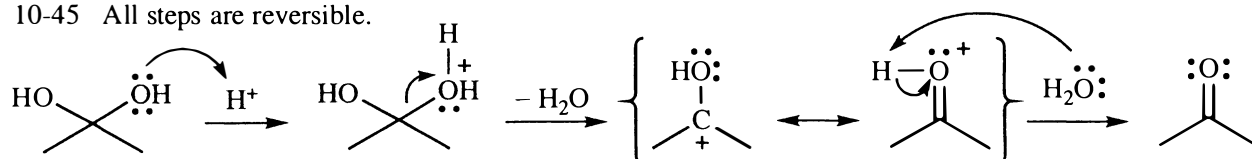
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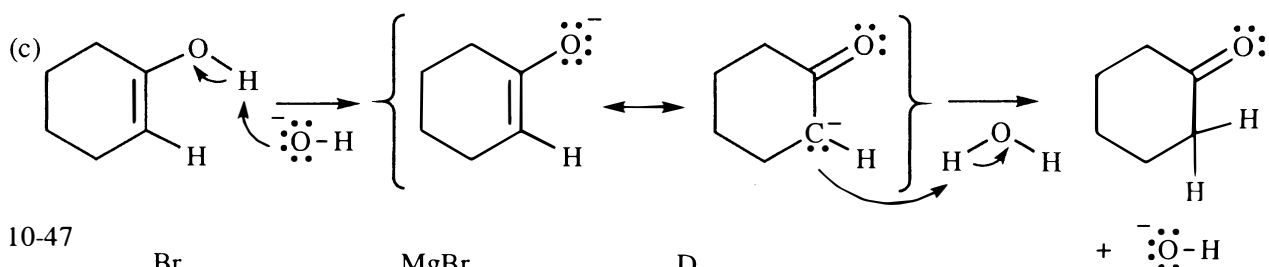
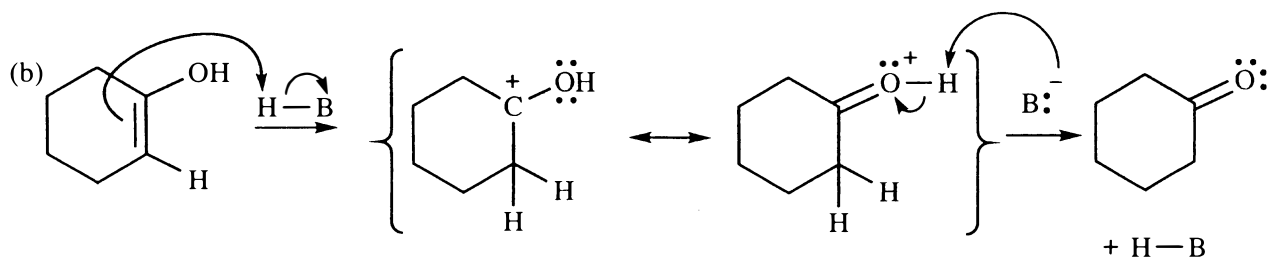
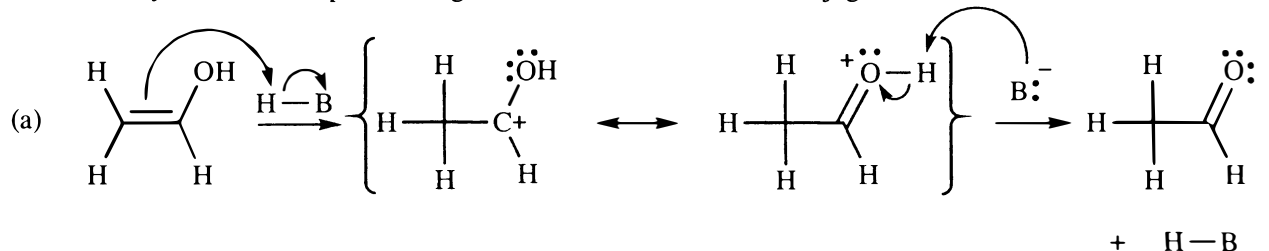
10-44 The goal is to synthesize the target compound (boxed) from starting materials of six carbons or fewer. The product has 12 carbons, so the logical "disconnection" in working backwards is two six carbon fragments which could be joined in a Grignard reaction. The best way to make epoxides is from the double bond, and double bonds are made from alcohols which are the products of Grignard reactions.



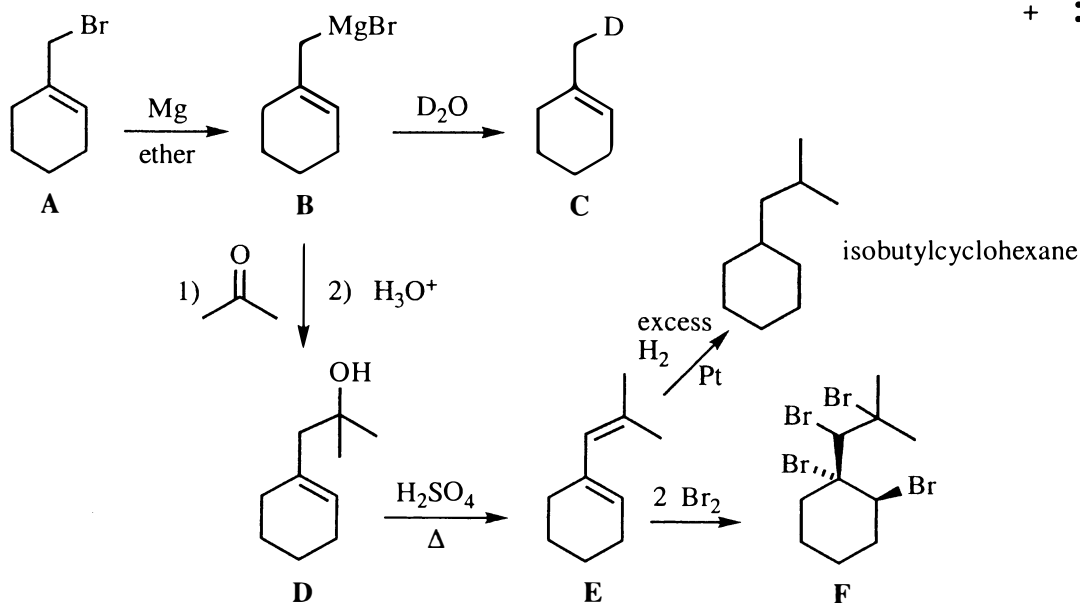
10-45 All steps are reversible.



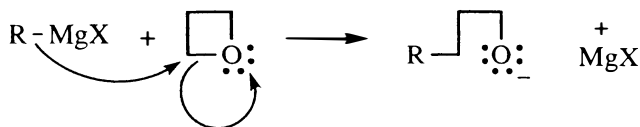
10-46 The symbol $\text{H}-\text{B}$ represents a generic acid, where B^- is the conjugate base.



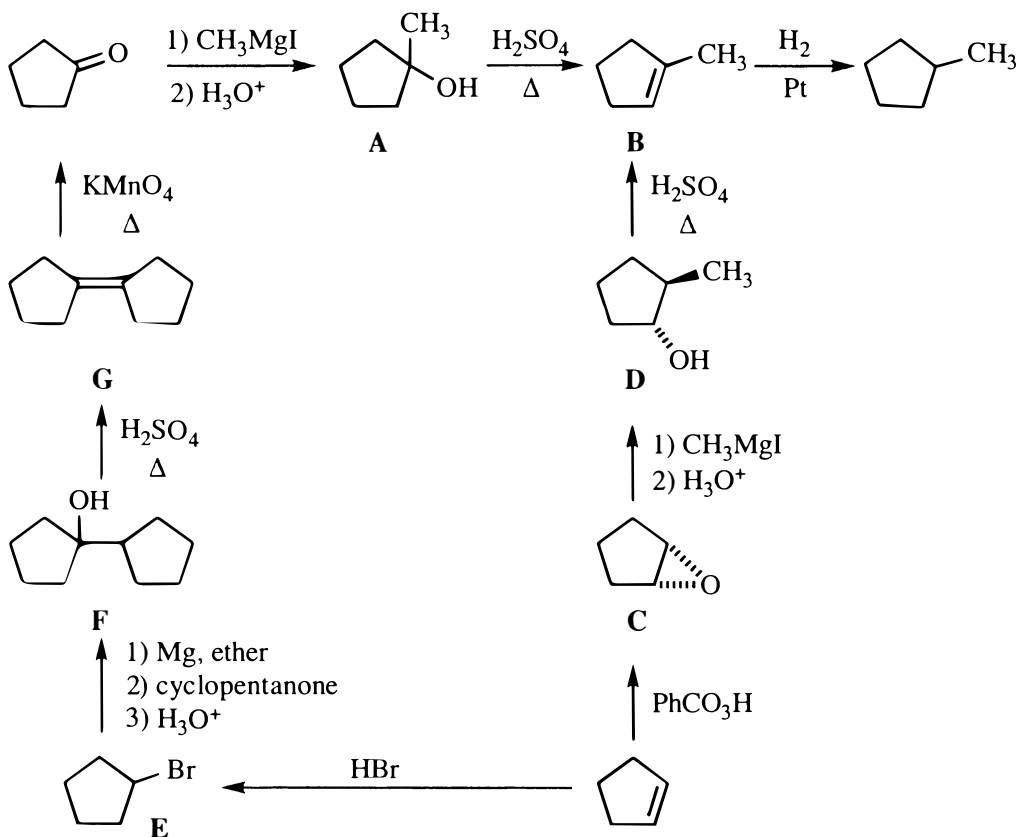
10-47



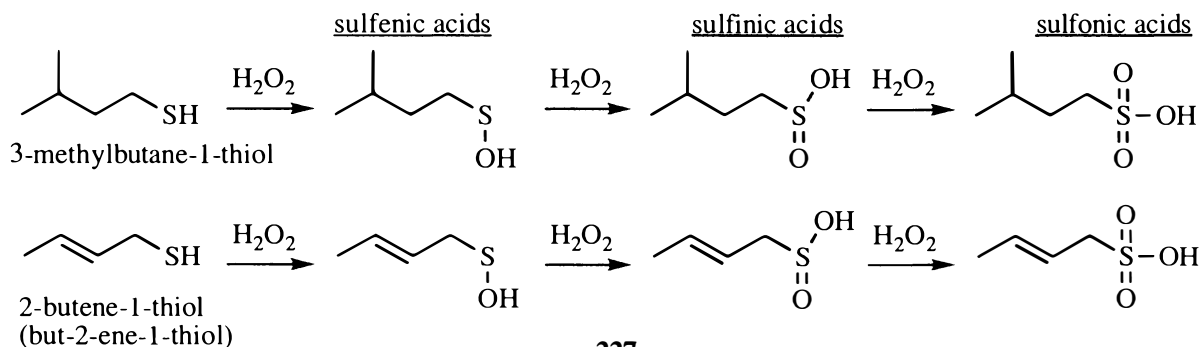
10-48 This mechanism is similar to cleavage of the epoxide in ethylene oxide by Grignard reagents. The driving force for the reaction is relief of ring strain in the 4-membered cyclic ether, which is why it will undergo a Grignard reaction whereas most other ethers will not.

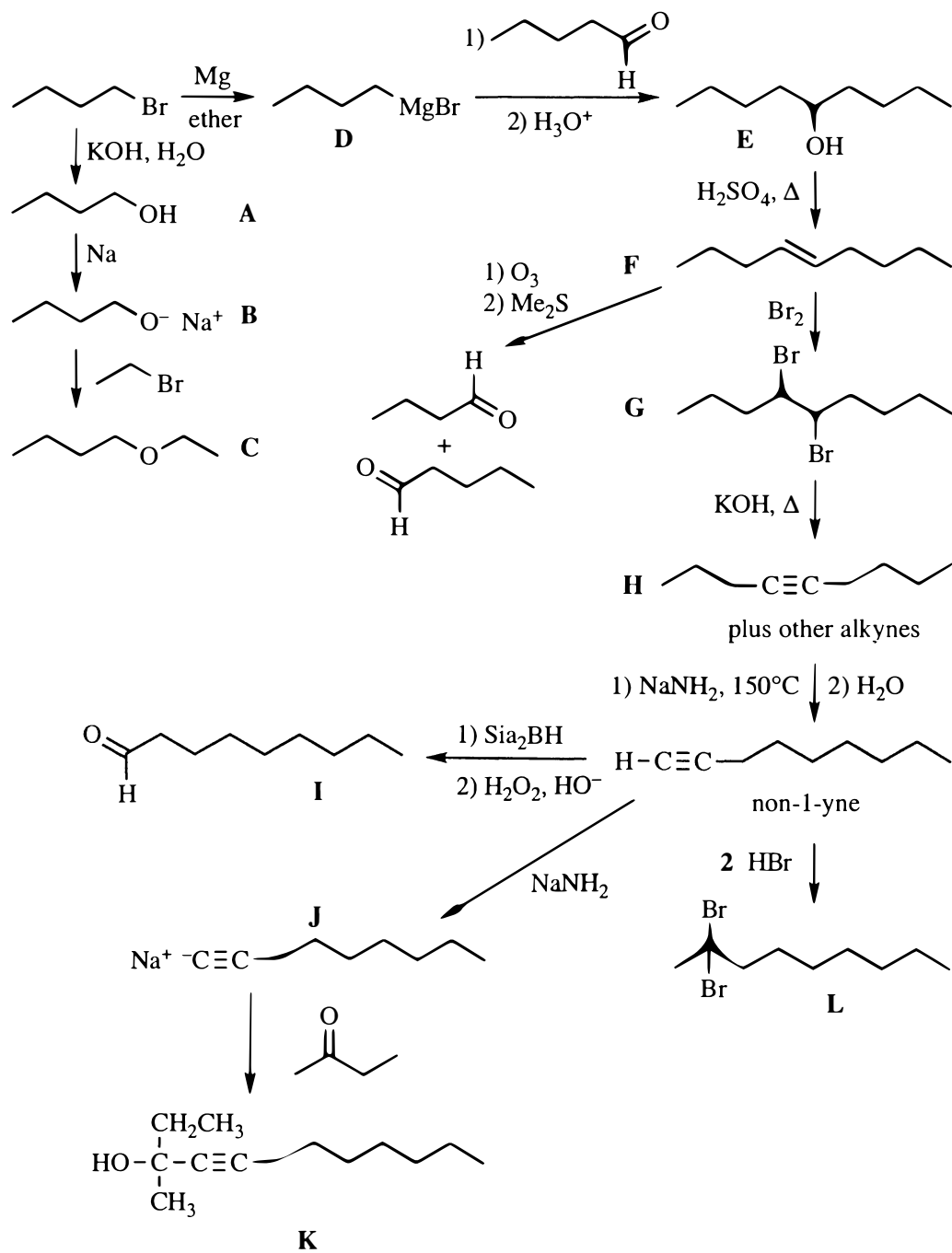


10-49 When mixtures of isomers can result, only the major product is shown.



10-50 The most important reactant in the desking mixture is hydrogen peroxide. Thiols are oxidized to structures having one, two, or three oxygens on the sulfur; all of these functional groups are acidic. The sodium bicarbonate is basic enough to ionize these acids, making them water soluble where the soap can wash them away.



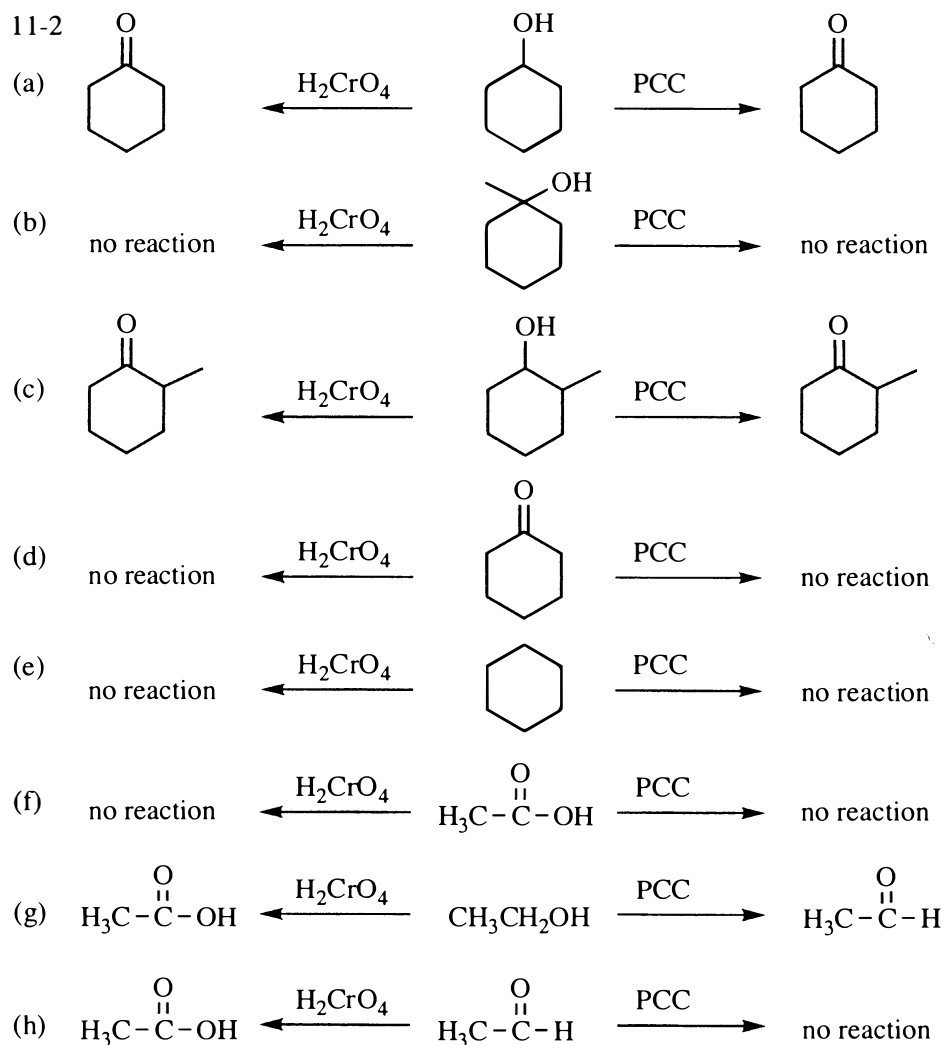


CHAPTER 11—REACTIONS OF ALCOHOLS

11-1

- (a) both reactions are oxidations
- (b) oxidation, oxidation, reduction, oxidation
- (c) one carbon is oxidized and one carbon is reduced—no net change
- (d) reduction: C—O is replaced by C—H
- (e) neither oxidation nor reduction—the C still has two bonds to O
- (f) oxidation (addition of X₂)
- (g) neither oxidation nor reduction (addition of HX)
- (h) neither oxidation nor reduction (elimination of H₂O)
- (i) oxidation: adding an O to each carbon of the double bond
- (j) the first reaction is oxidation as a new C—O bond is formed to each carbon of the alkene; the second reaction is neither oxidation nor reduction, as H₂O is added to the epoxide, and each carbon still has one bond to oxygen
- (k) neither oxidation nor reduction: H—B is added in the first reaction, and B is replaced by O in the second reaction; overall, only H and OH are added, so there is no net oxidation nor reduction. (Note that in functional groups involving two carbons like alkenes or alkynes, both carbons have to be oxidized or reduced before the *net* change to the functional group is classified as oxidation or reduction.)

11-2



11-3

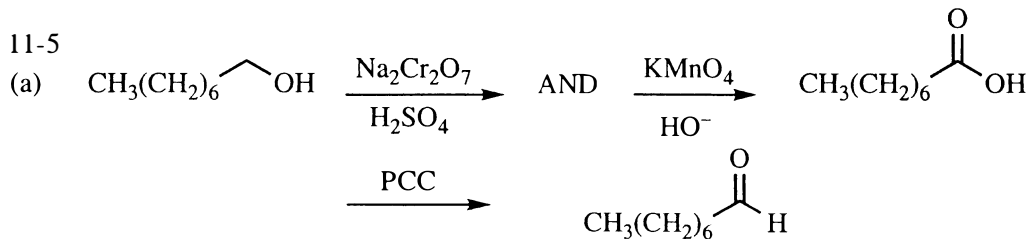
(a) A 1° alcohol loses two hydrogens when transformed to the aldehyde, and a 2° alcohol loses one hydrogen in forming a ketone; each alcohol is oxidized. DMSO loses an oxygen from the sulfur; it is clearly reduced. (If you got those two, you did the problem correctly.) To be rigorous, oxalyl chloride undergoes a disproportionation reaction: one C is oxidized to CO₂ and the other C is reduced to CO; however, the net effect on the elements in oxalyl chloride is "no change".

(b) Text section 8-15B shows that dimethyl sulfide reduces an ozonide. In the process, dimethyl sulfide is oxidized to DMSO.

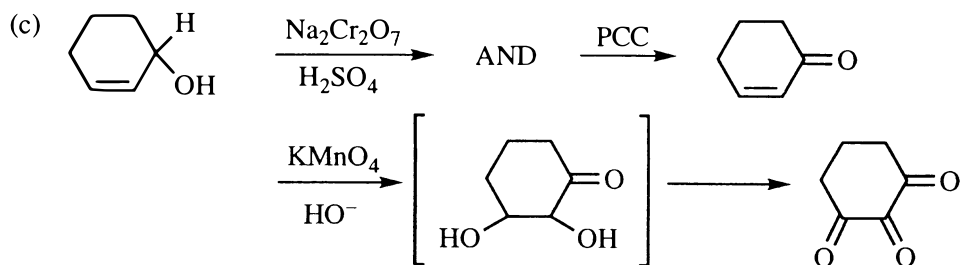
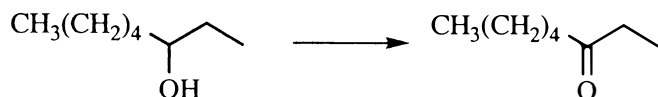
11-4

(a) Dehydrogenation does not occur at 25° C—either: 1) there is a high kinetic barrier (a high activation energy) for this reaction, or 2) it is thermodynamically unfavorable, with $\Delta G > 0$. The latter possibility is supported by the fact that the reverse reaction (catalytic hydrogenation of a carbonyl) is spontaneous at 25° C (see text section 10-11C) and therefore has $\Delta G < 0$. This makes the question of kinetics academic—a reaction that cannot proceed must be uselessly slow.

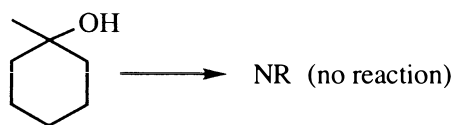
(b) and (c) Kinetics will improve with increasing temperature for virtually all reactions, so both the hydrogenation and dehydrogenation reactions will go faster. In this case, however, the question is how to favor the dehydrogenation reaction. The answer is that thermodynamics will favor this reaction as the temperature is raised. The key is the fundamental thermodynamic equation $\Delta G = \Delta H - T\Delta S$. We can estimate that $\Delta H > 0$ since the product ketone plus hydrogen is less stable than the starting alcohol. Also, $\Delta S > 0$ since one molecule is converted to two: therefore, $-T\Delta S < 0$. At low temperature (25° C), ΔH dominates because T is so small, so $\Delta G > 0$. At a high enough temperature, the $-T\Delta S$ term will begin to overwhelm ΔH , and ΔG will become negative. For the reaction in question, this must be the case at 300° C.



(b) all three reagents give the same ketone product with a secondary alcohol



(d) all three reagents give no reaction with a tertiary alcohol

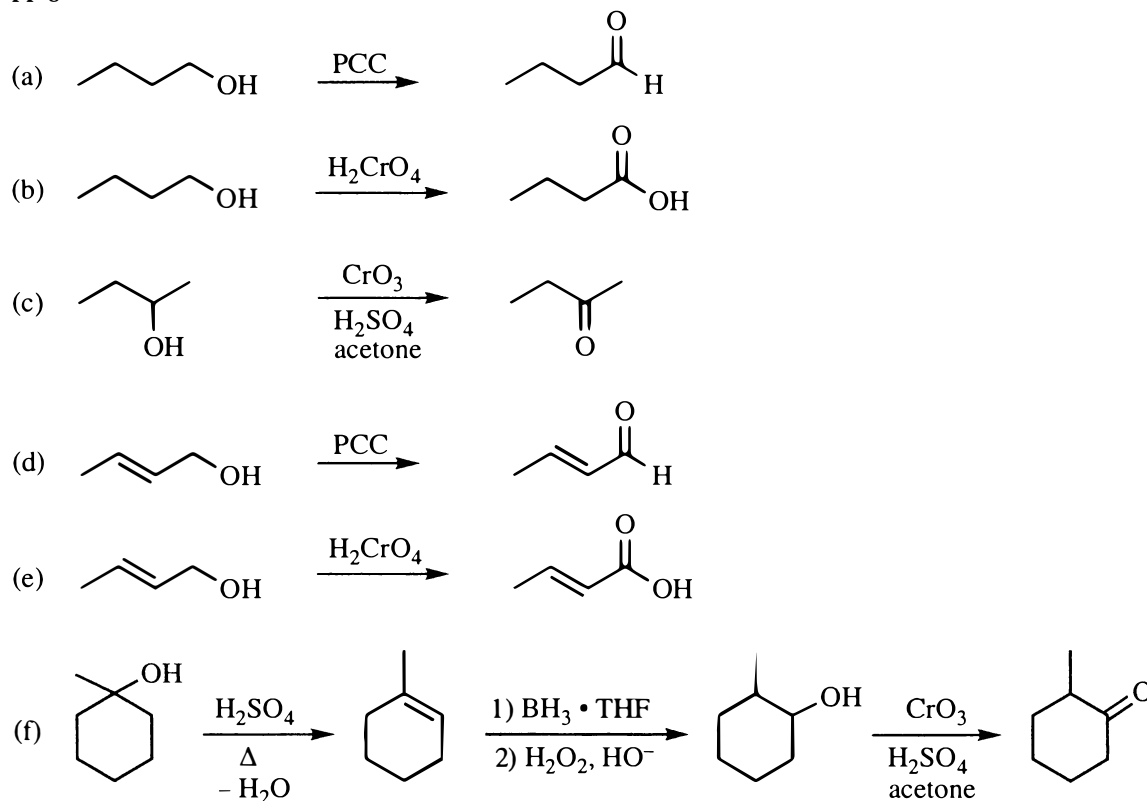


Note to the student: For simplicity, this book will use these standard laboratory methods of oxidation:

- PCC (pyridinium chlorochromate) to oxidize 1° alcohols to aldehydes;
- H₂CrO₄ (chromic acid) to oxidize 1° alcohols to carboxylic acids;
- CrO₃, H₂SO₄, acetone (Jones reagent) to oxidize 2° alcohols to ketones.

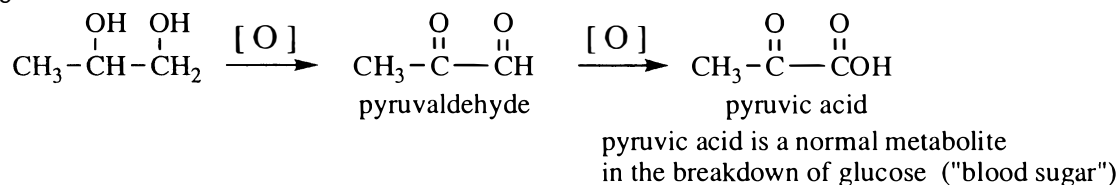
Understand that other choices are legitimate; for example, Swern oxidation works about as well as PCC in the preparation of aldehydes, and Collins reagent or PCC will oxidize a 2° alcohol to a ketone as well as chromic acid. If you have a question about the appropriateness of a reagent you choose, consult the table in the text before Problem 11-2.

11-6

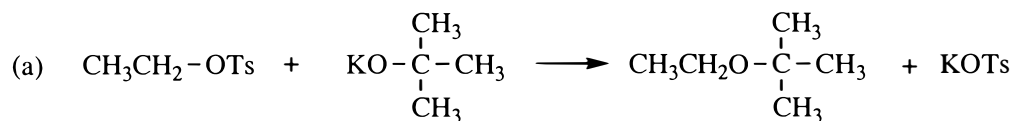
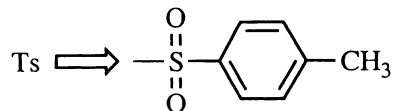


11-7 A chronic alcoholic has induced more ADH enzyme to be present to handle large amounts of imbibed ethanol, so requires more ethanol "antidote" molecules to act as a competitive inhibitor to "tie up" the extra enzyme molecules.

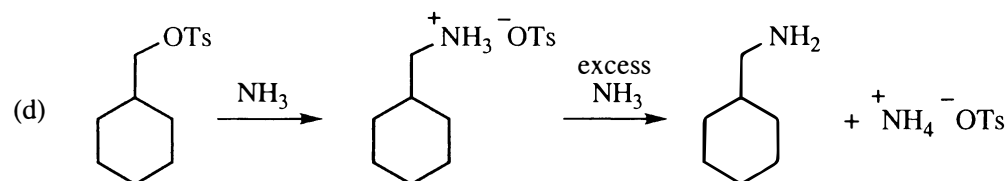
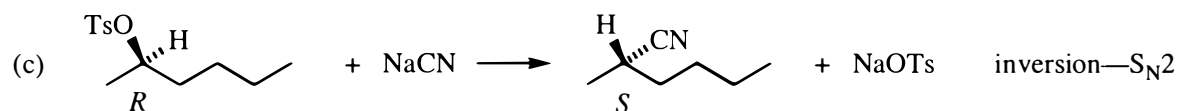
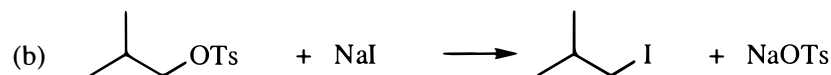
11-8



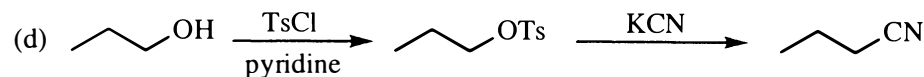
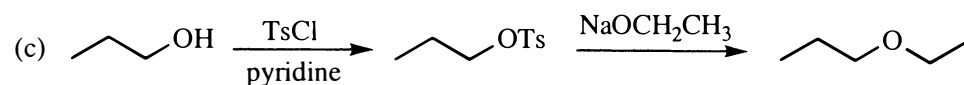
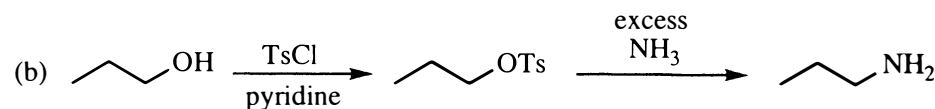
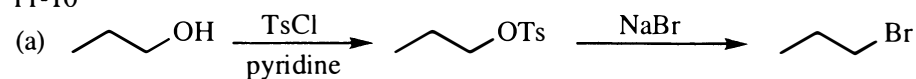
11-9 From this problem on, "Ts" will refer to the "tosyl" or "*p*-toluenesulfonyl" group:



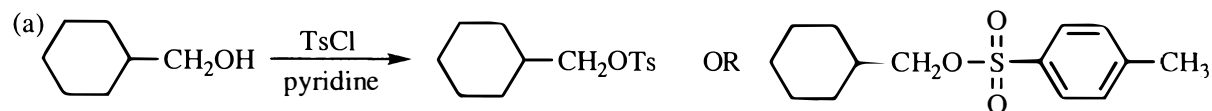
(E2 is also possible with this hindered base; the product would be ethylene, $\text{CH}_2=\text{CH}_2$.)



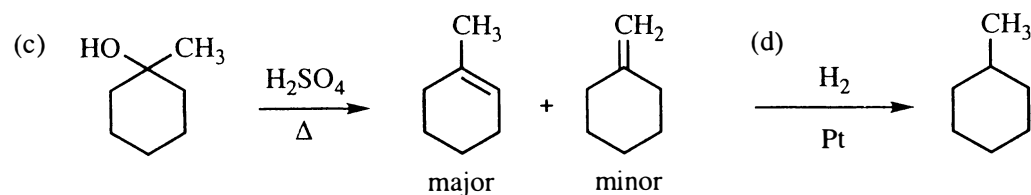
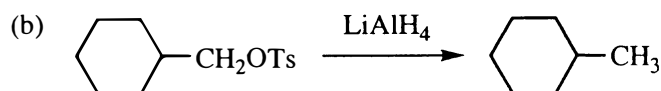
11-10



11-11

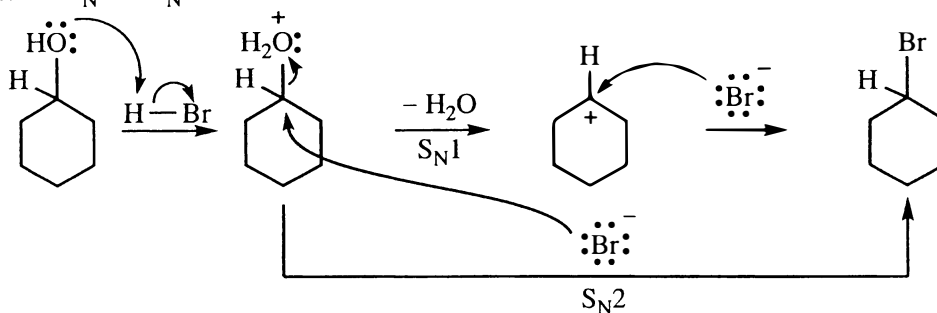


11-11 continued

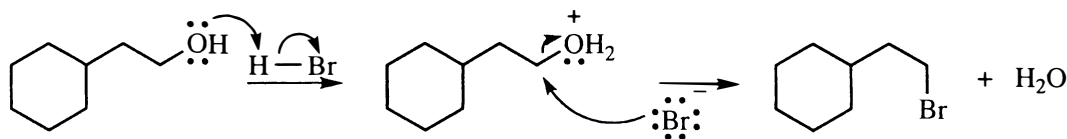


11-12

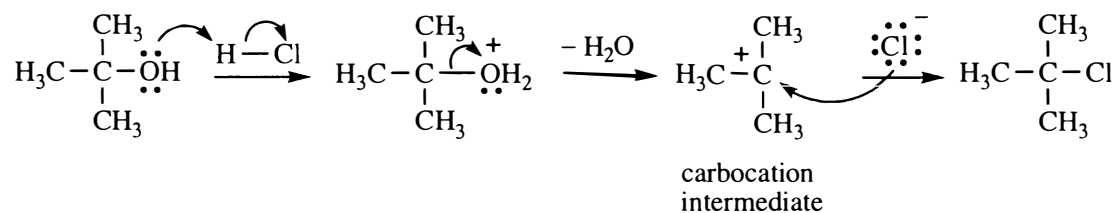
(a) either S_N1 or S_N2 on 2° alcohols



(b) S_N2 on 1° alcohols

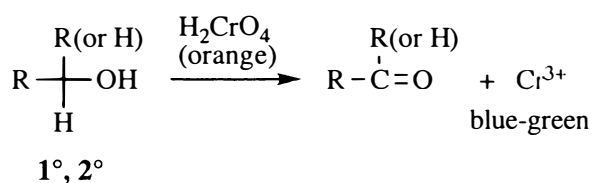
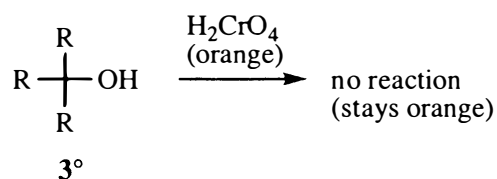


11-13



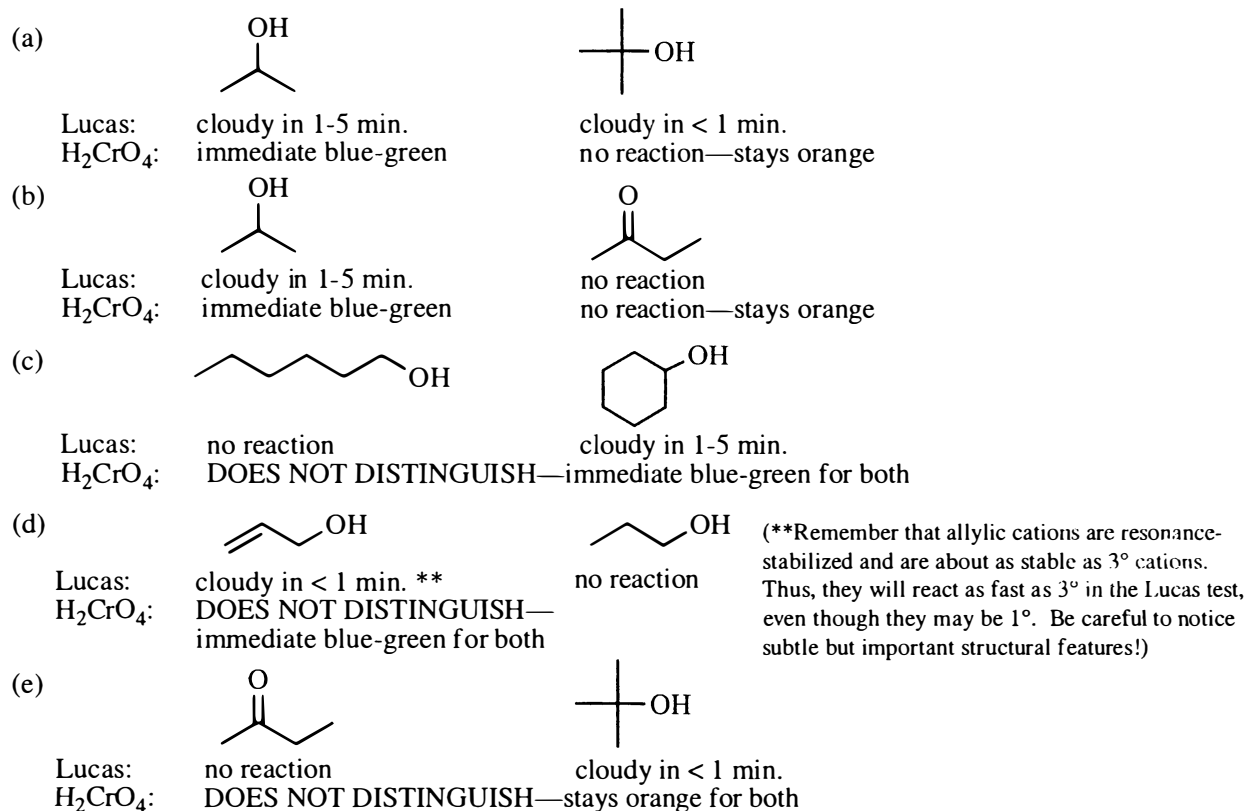
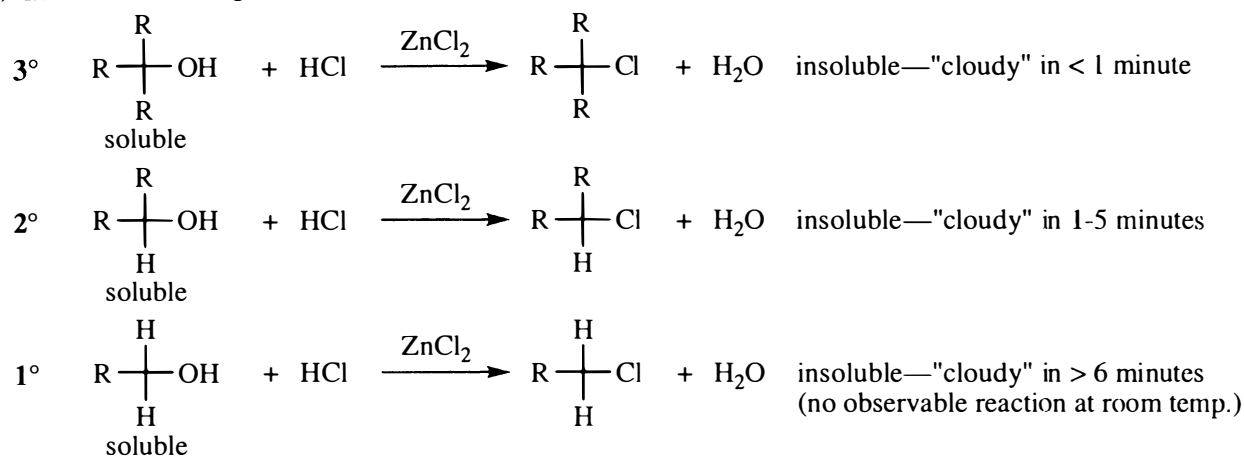
11-14 The two standard qualitative tests are:

1) chromic acid—distinguishes 3° alcohol from either 1° or 2°

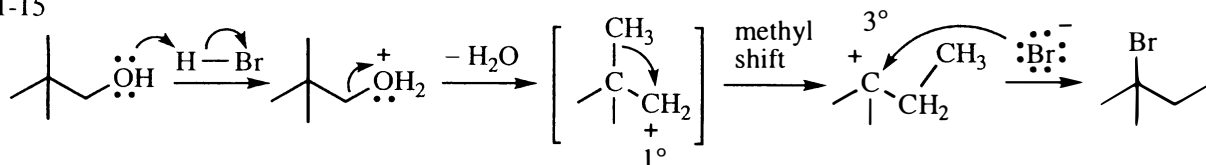


11-14 continued

2) Lucas test—distinguishes 1° from 2° from 3° alcohol by the rate of reaction

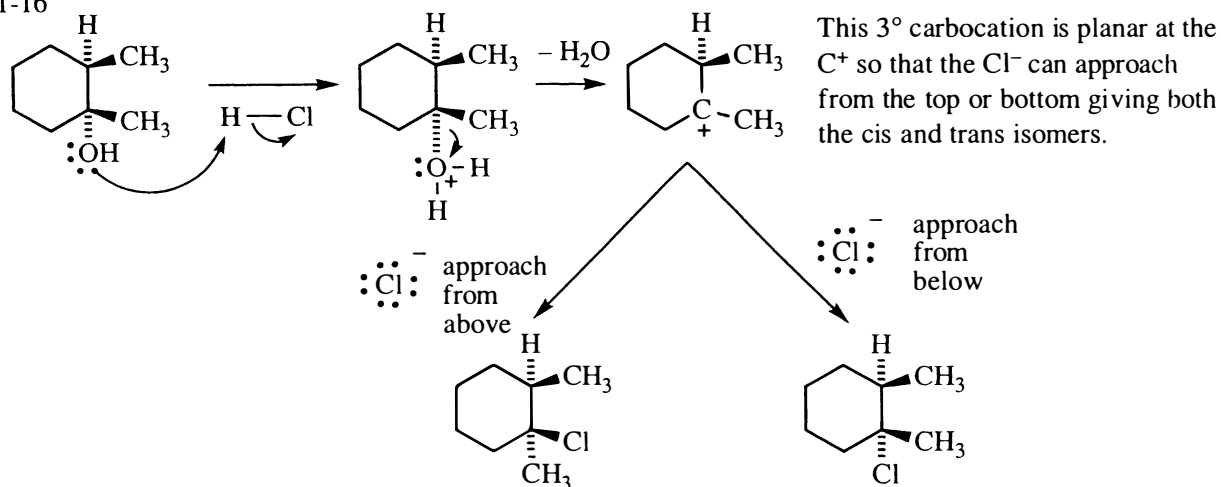


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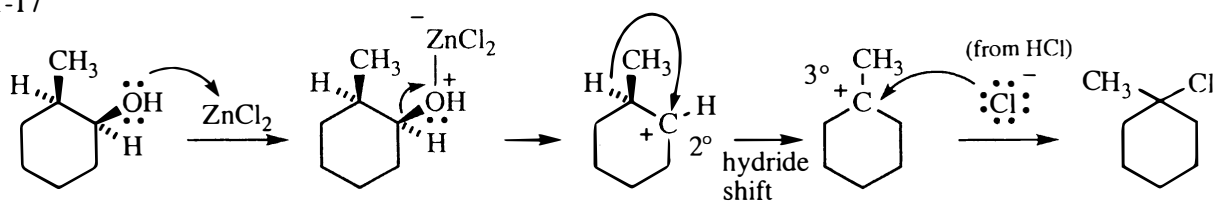


Even though 1°, the neopentyl carbon is hindered to backside attack, so S_N2 cannot occur easily. Instead, an S_N1 mechanism occurs, with rearrangement.

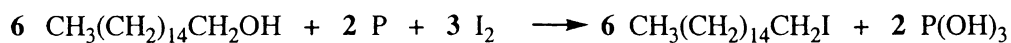
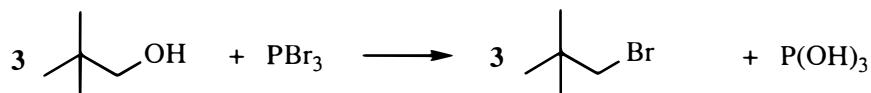
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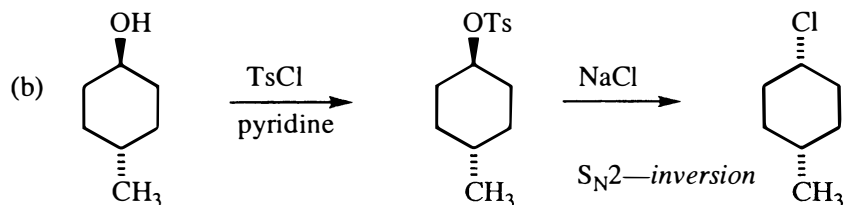
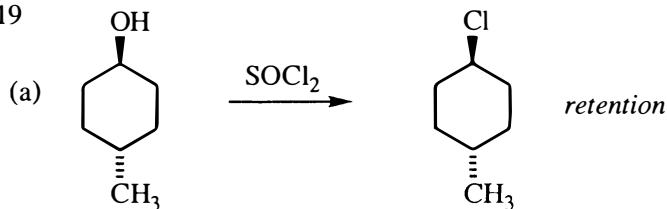
11-17



11-18



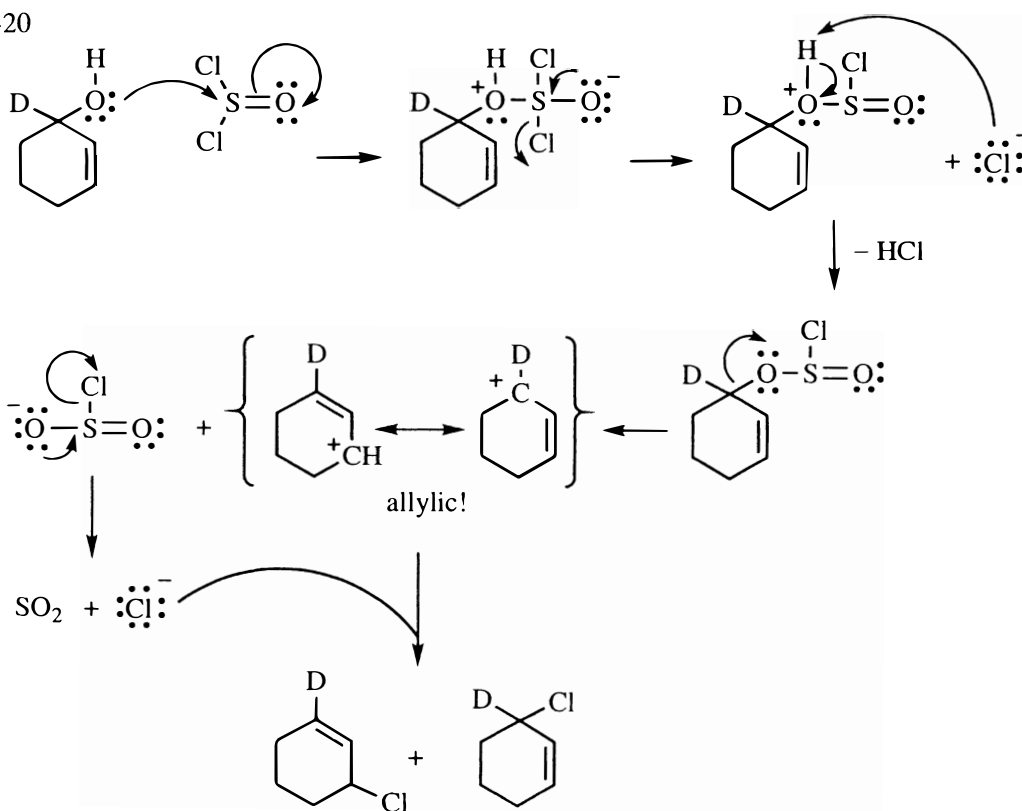
11-19



Another possible answer would be to use PCl₃.

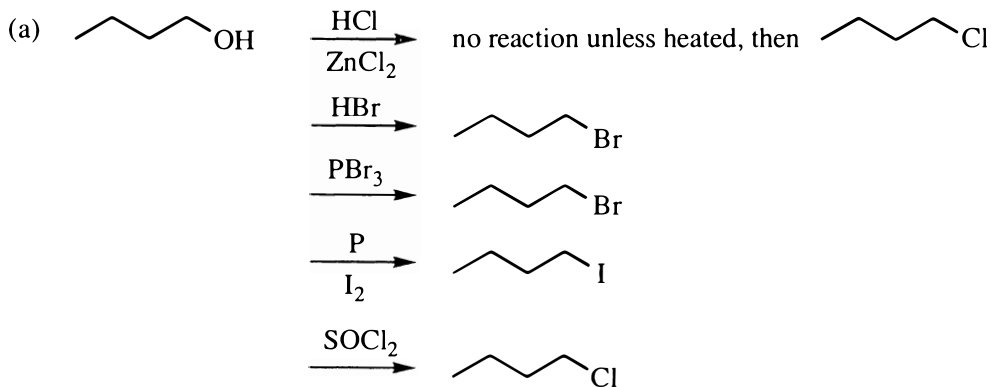
11-20

(a)

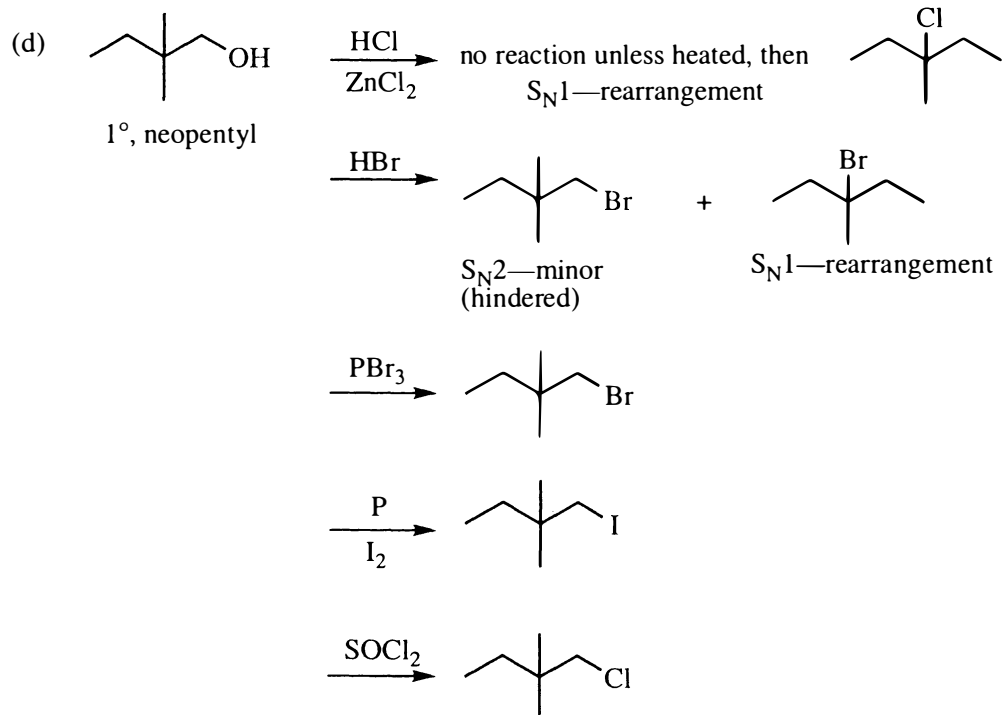
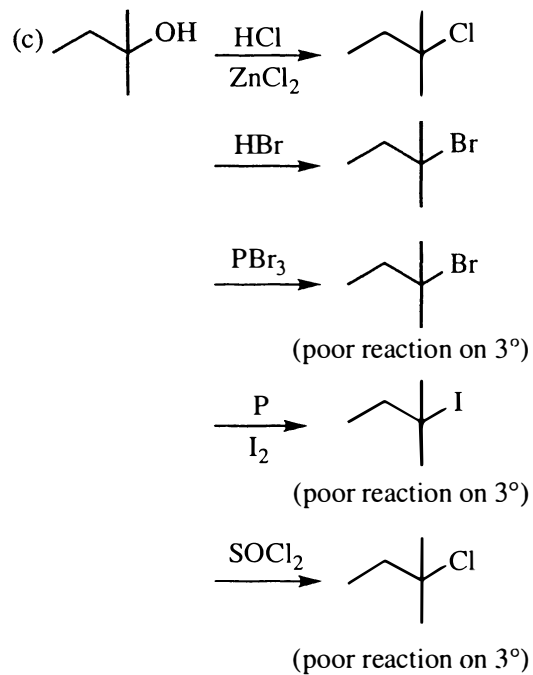
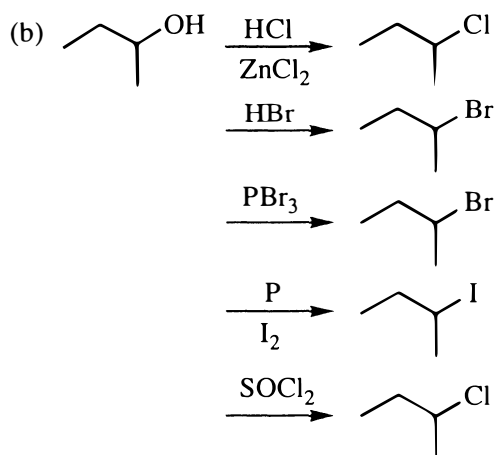


(b) The key is that the intermediate carbocation is allylic, very stable and relatively long-lived. It can therefore escape the ion pair and become a "free carbocation". The nucleophilic chloride can attack any carbon with positive charge, not just the one closest. Since two carbons have partial positive charge, two products result.

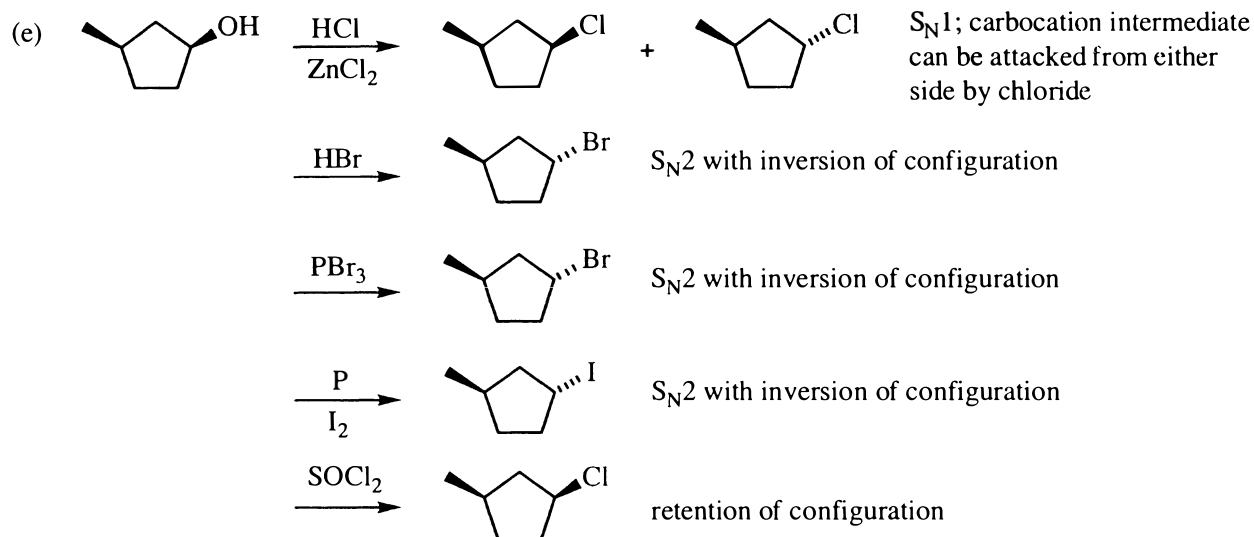
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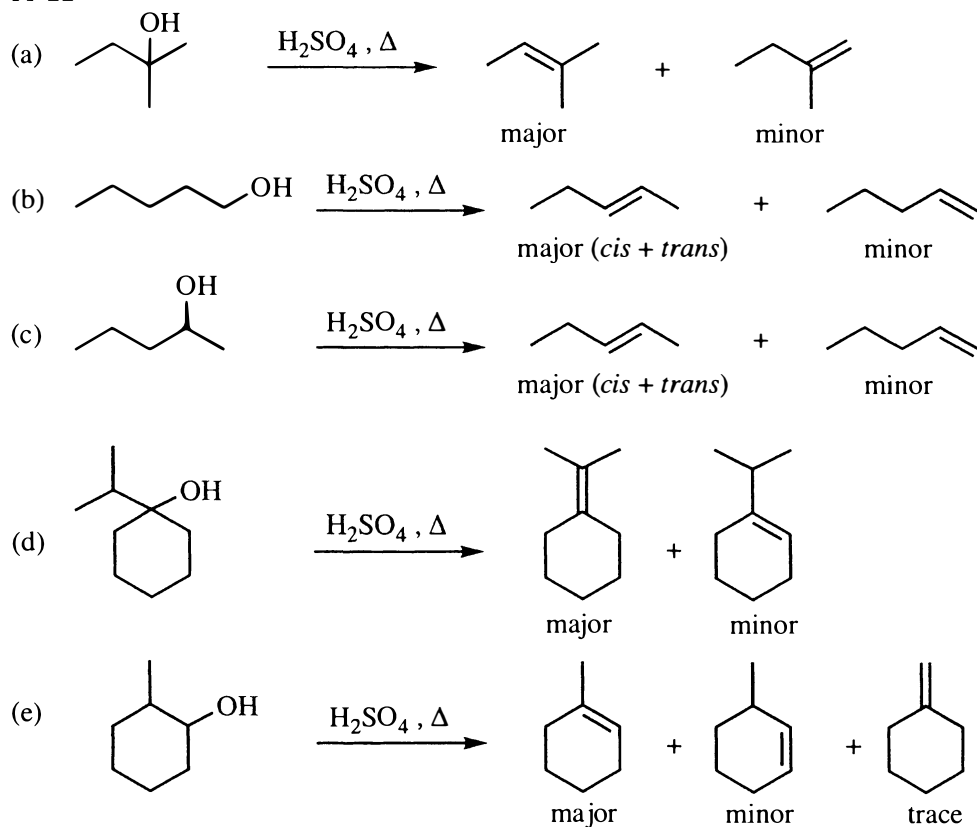
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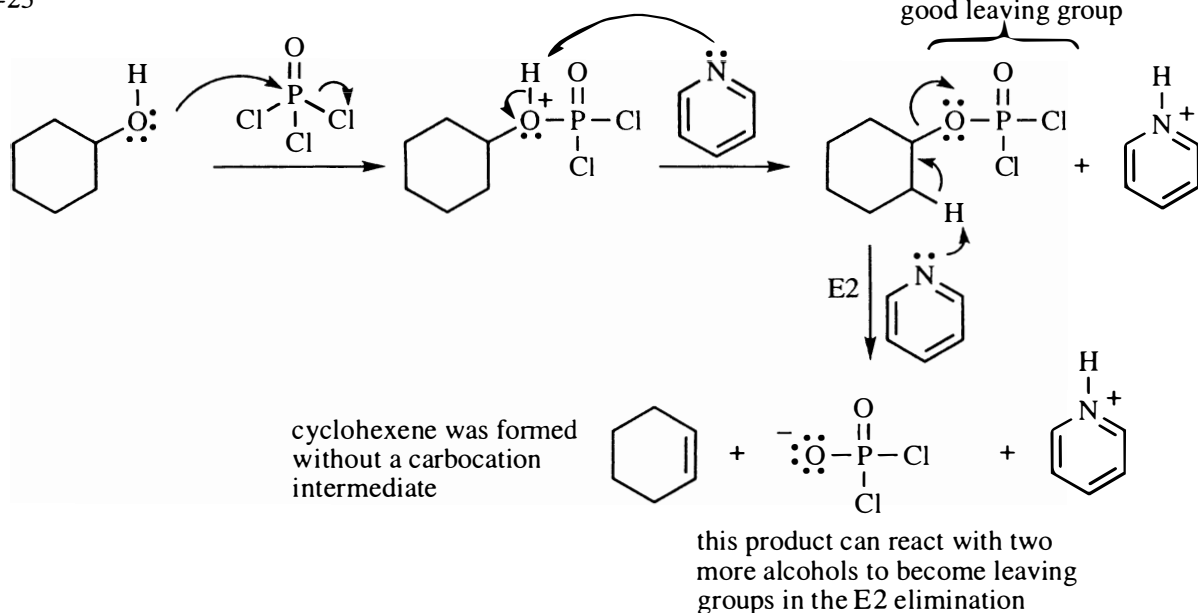
11-21 continued



11-22

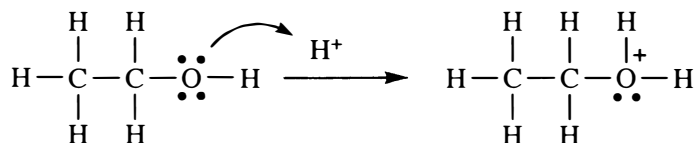


11-23

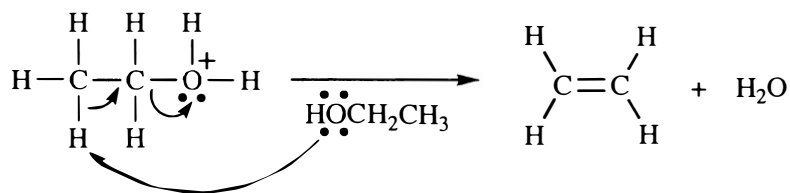


11-24

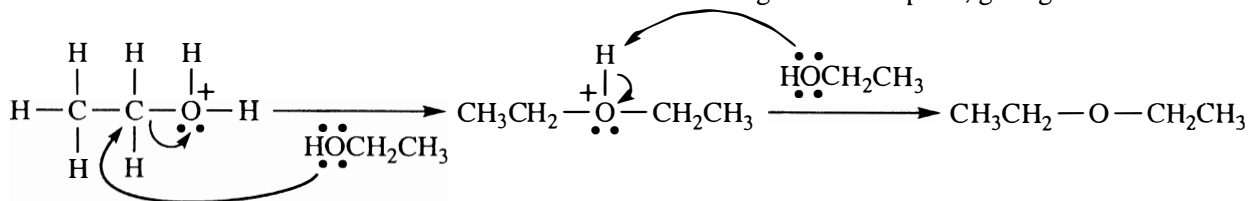
Both mechanisms begin with protonation of the oxygen.



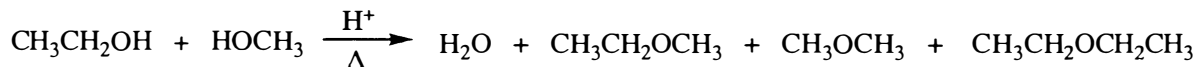
One mechanism involves another molecule of ethanol acting as a base, giving elimination.



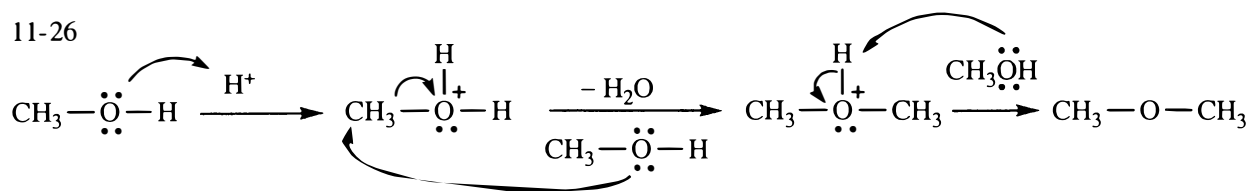
The other mechanism involves another molecule of ethanol acting as a nucleophile, giving substitution.



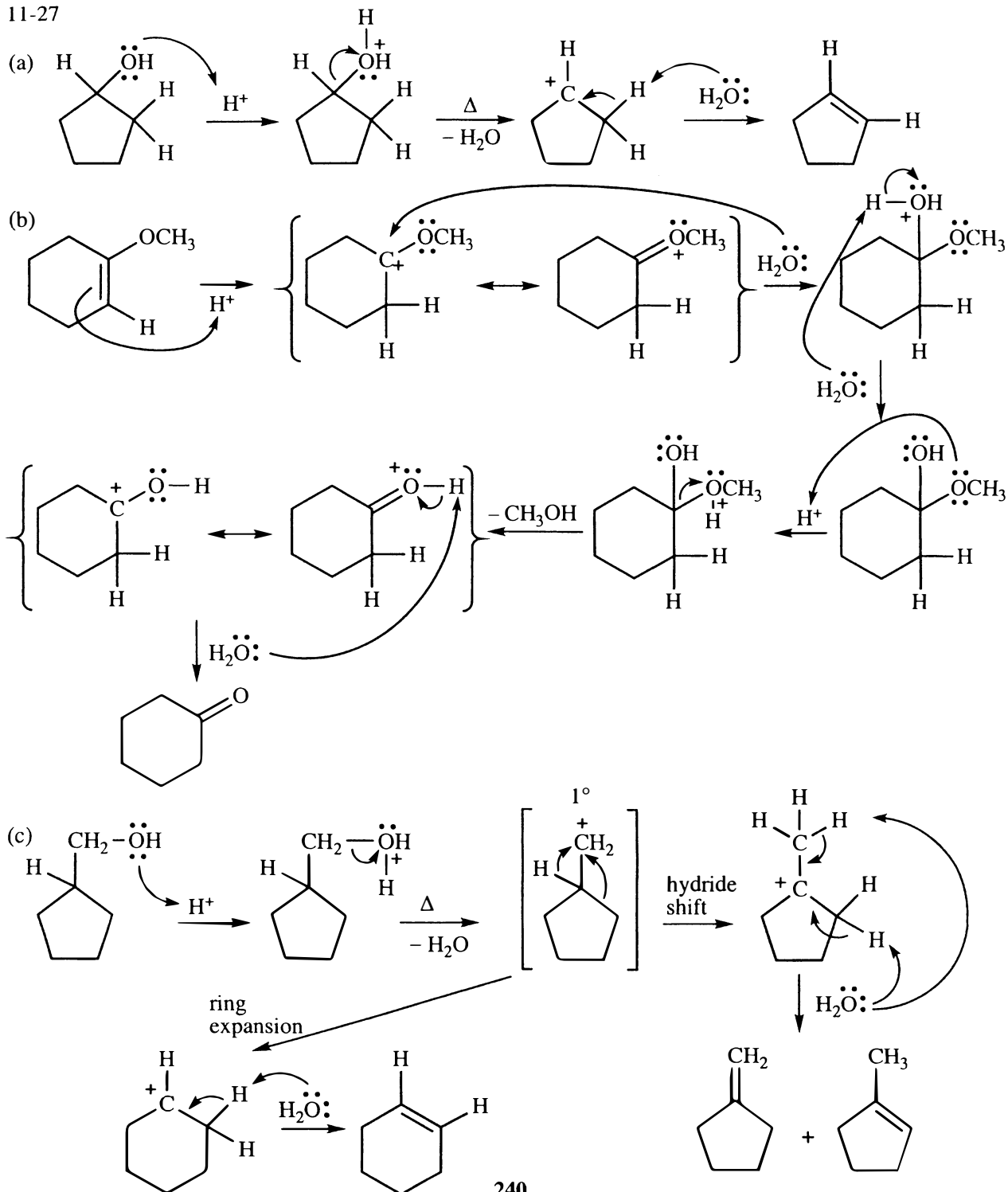
11-25 An equimolar mixture of methanol and ethanol would produce all three possible ethers. The difficulty in separating these compounds would preclude this method from being a practical route to any one of them. This method is practical only for symmetric ethers, that is, where both alkyl groups are identical.



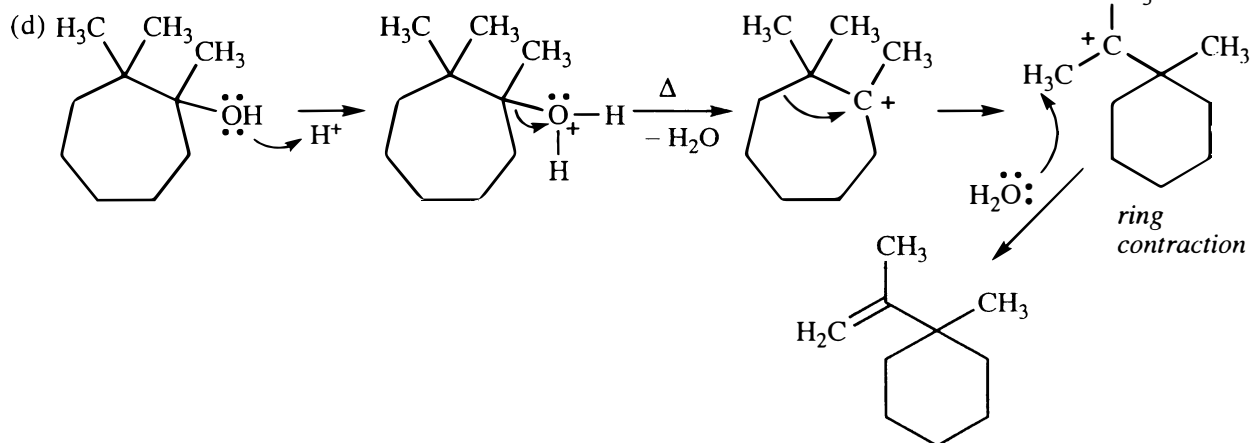
11-26



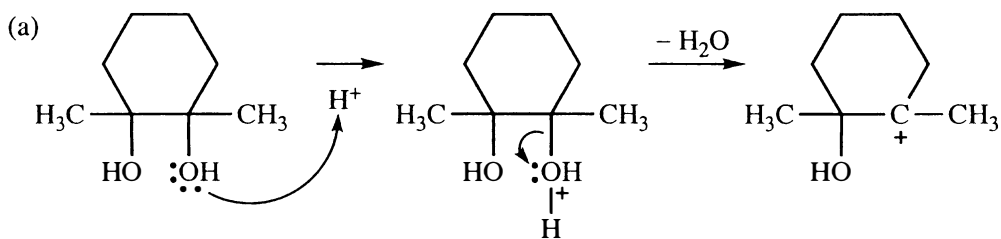
11-27



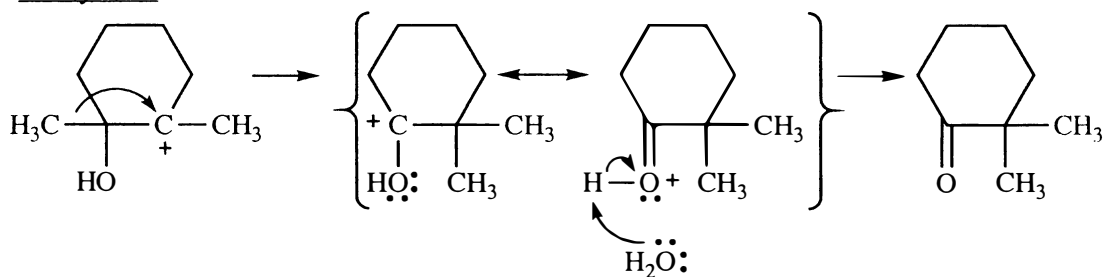
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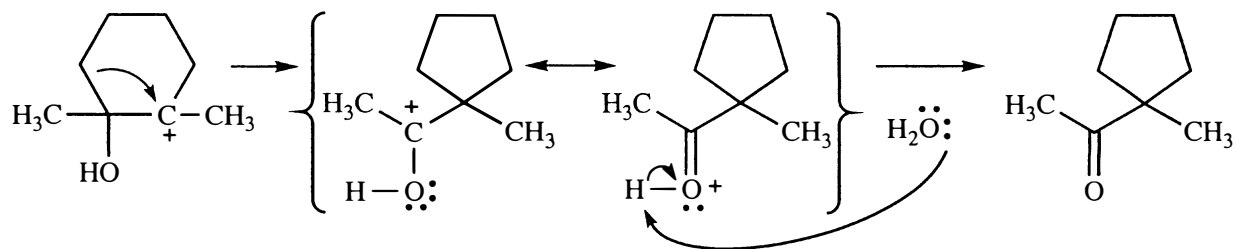
11-28



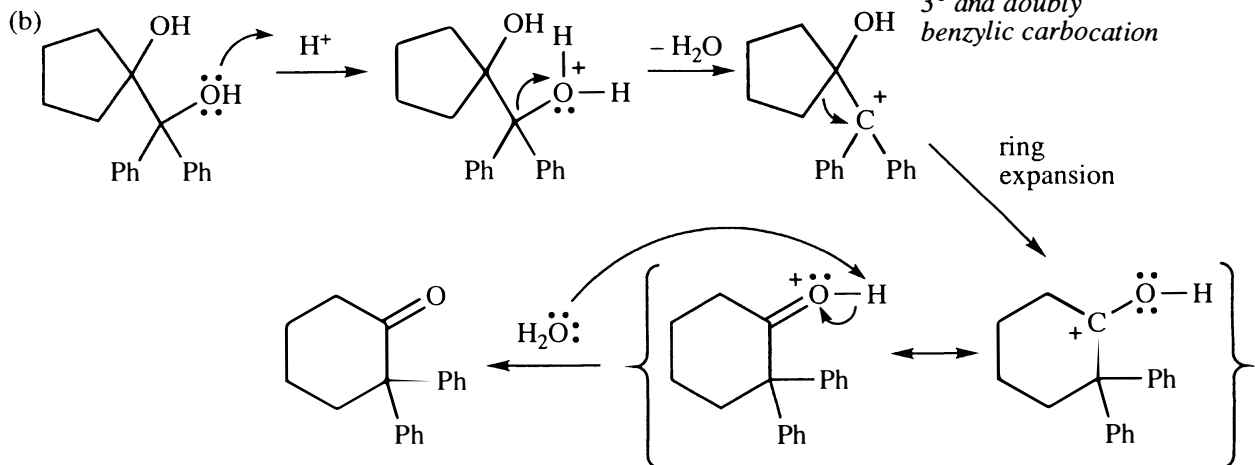
Methyl shift



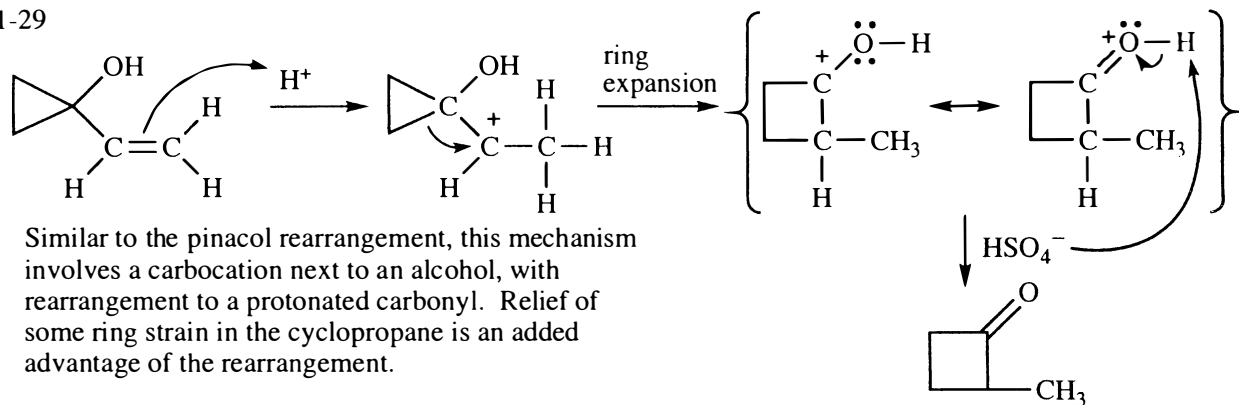
Alkyl shift—ring contraction



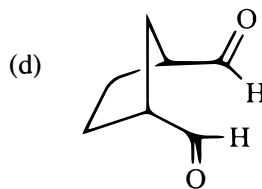
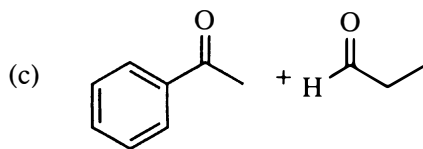
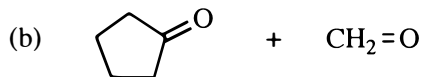
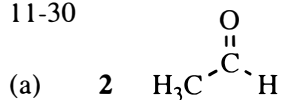
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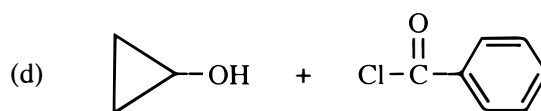
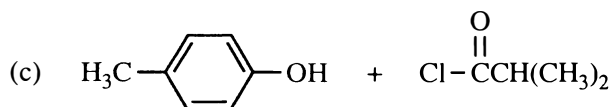
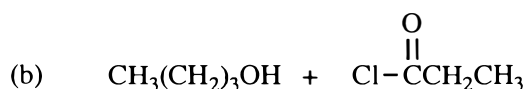
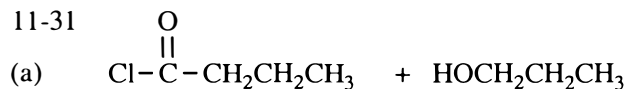
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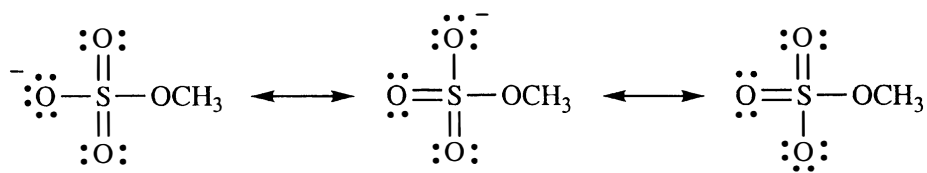
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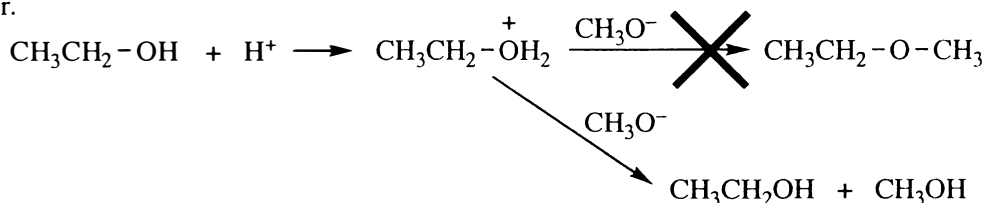
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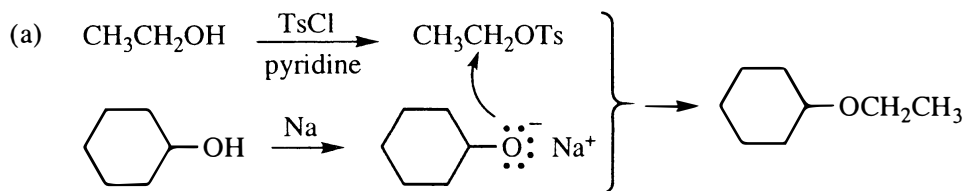
11-32



11-33 Proton transfer (acid-base) reactions are much faster than almost any other reaction. Methoxide will act as a base and remove a proton from the oxygen much faster than methoxide will act as a nucleophile and displace water.



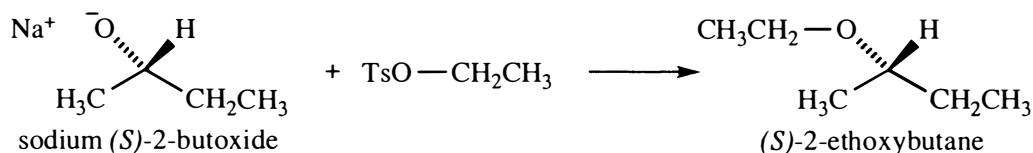
11-34



(b) There are two problems with this attempted bimolecular dehydration. First, all three possible ether combinations of cyclohexanol and ethanol would be produced. Second, hot sulfuric acid are the conditions for dehydrating secondary alcohols like cyclohexanol, so elimination would compete with substitution.

11-35

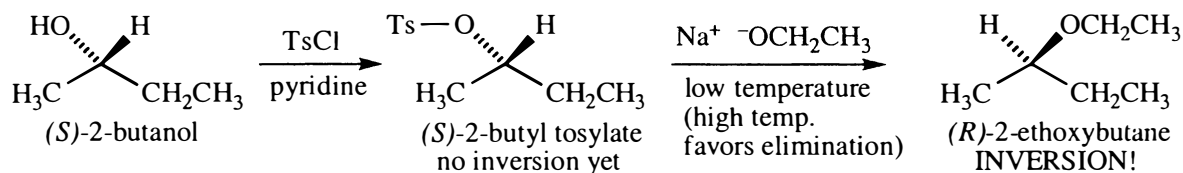
(a) What the student did:



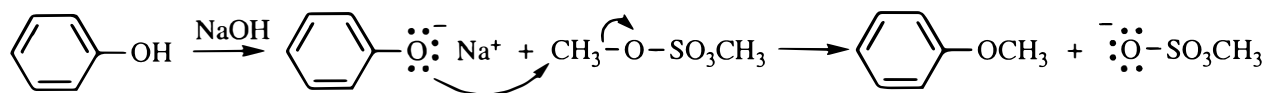
The product also has the *S* configuration, not the *R*. Why? The substitution is indeed an $\text{S}_{\text{N}}2$ reaction, but the *substitution did not take place at the chiral center*, so the configuration of the starting material is retained, not inverted.

(b) There are two ways to make (*R*)-2-ethoxybutane. Start with (*R*)-2-butanol, make the anion, and substitute on ethyl tosylate similar to part (a), or do an $\text{S}_{\text{N}}2$ inversion at the chiral center of (*S*)-2-butanol. $\text{S}_{\text{N}}2$ works better at 1° carbons so the former method would be preferred to the latter.

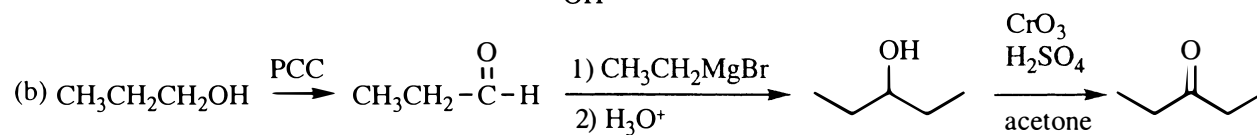
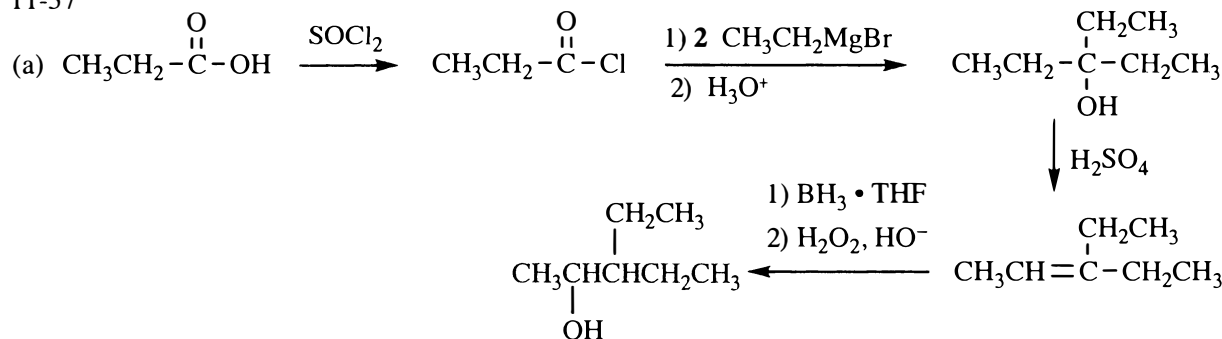
(c) This is not the optimum method because it requires $\text{S}_{\text{N}}2$ at a 2° carbon, as discussed in part (b).



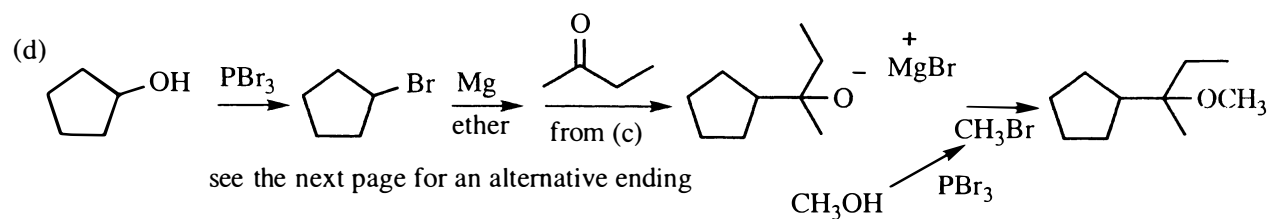
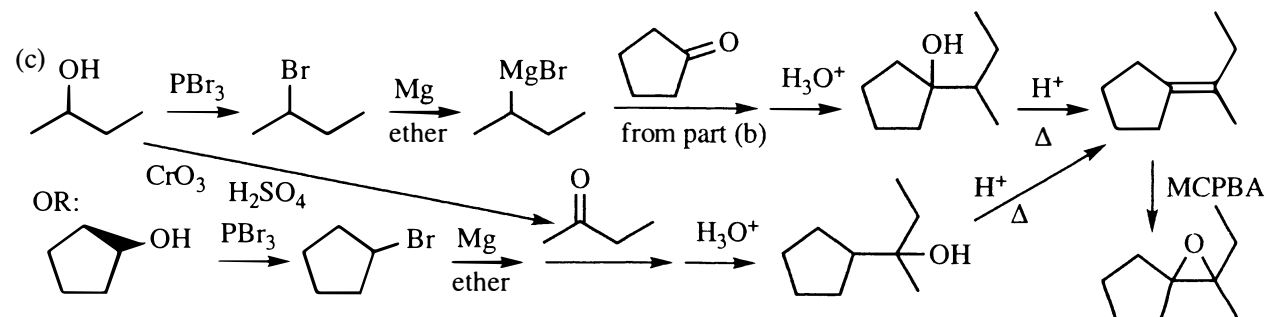
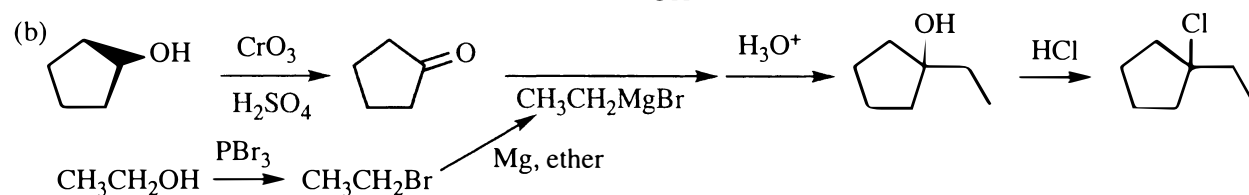
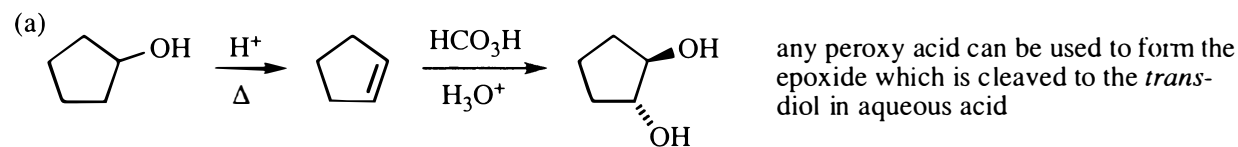
11-36



11-37

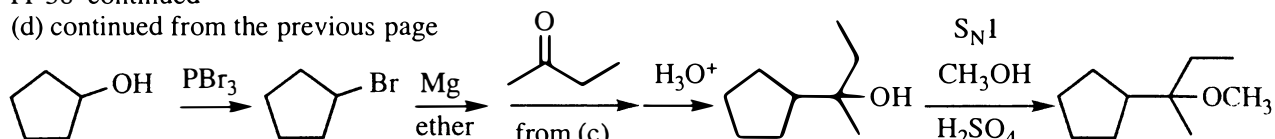


11-38

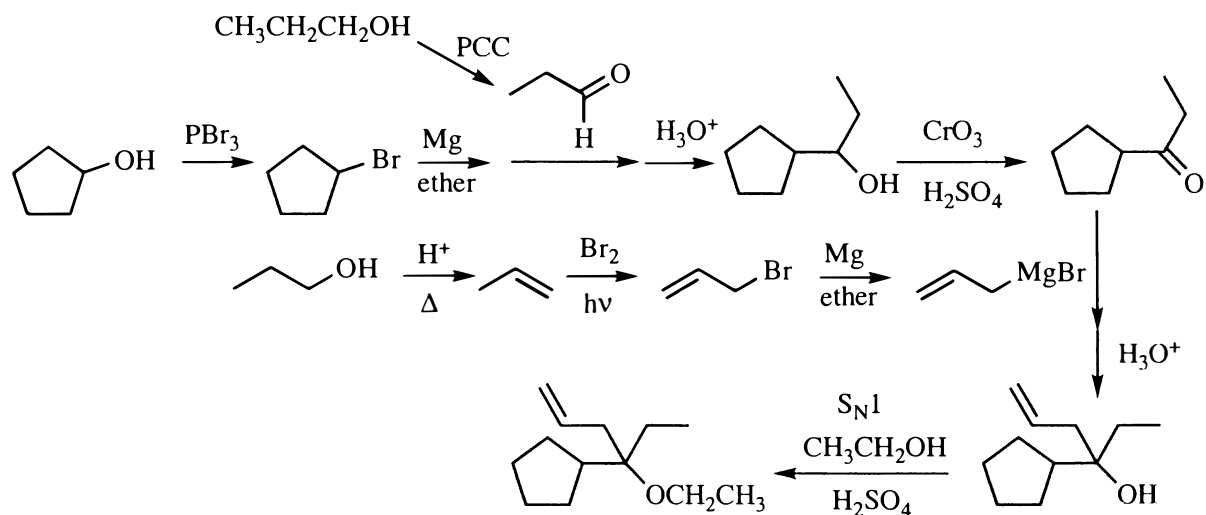


11-38 continued

(d) continued from the previous page

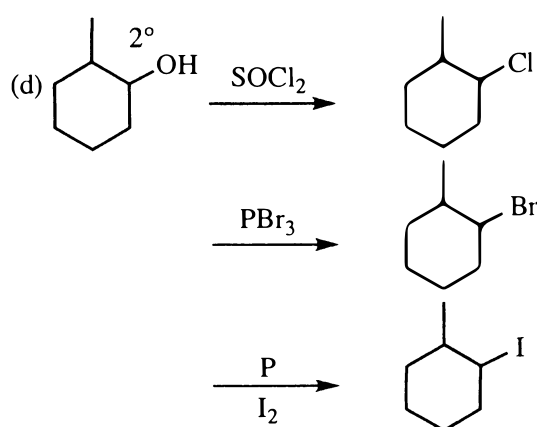
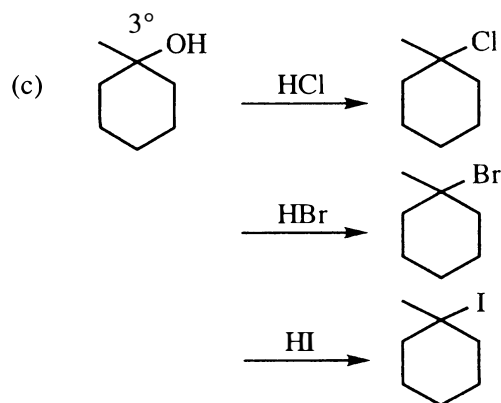
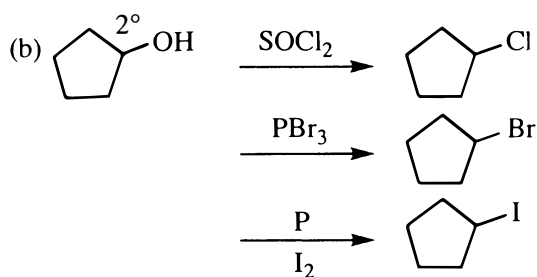
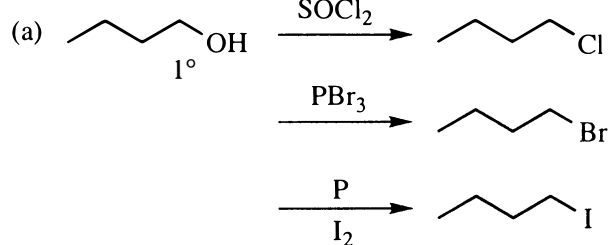


(e) There are several possible combinations of Grignard reactions on aldehydes or ketones. This is one example. Your example may be different and still be correct.

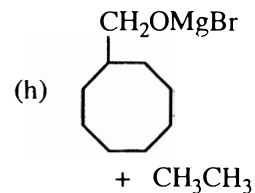
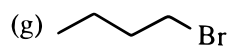
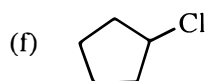
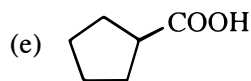
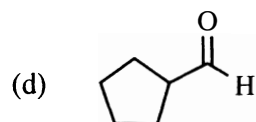
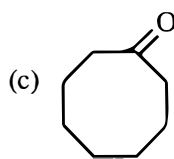
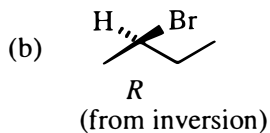
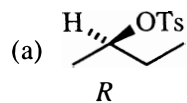
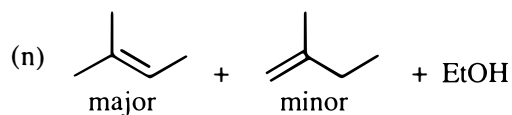
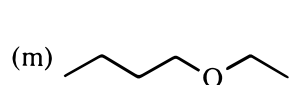
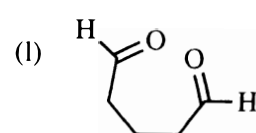
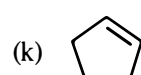
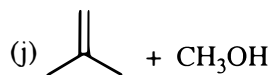
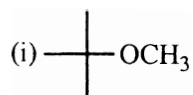


11-39 Please refer to solution 1-20, page 12 of this Solutions Manual.

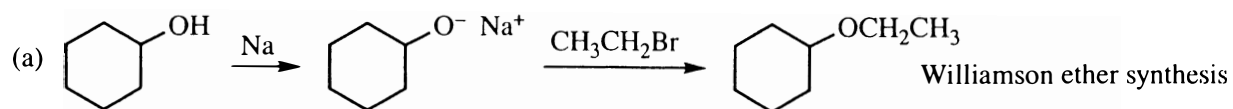
11-40



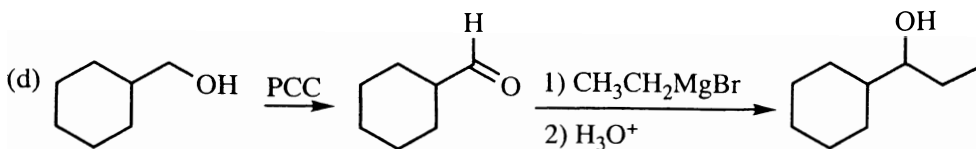
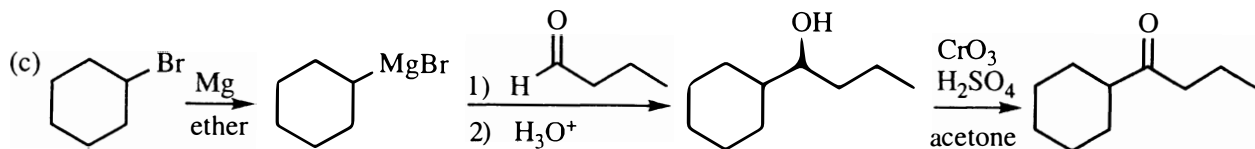
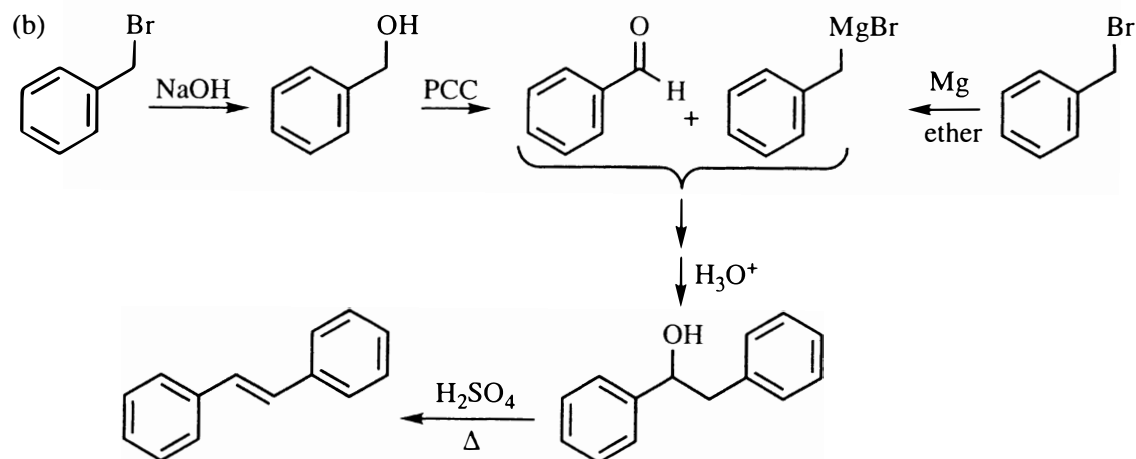
11-41

+ CH₃CH₃

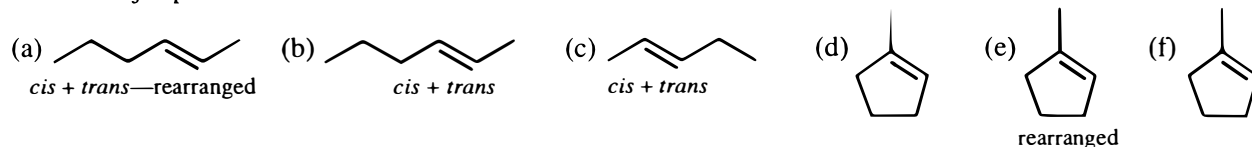
11-42



Williamson ether synthesis

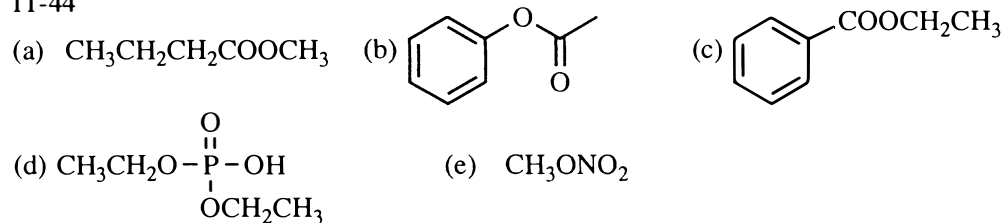


11-43 Major product for each reaction is shown.

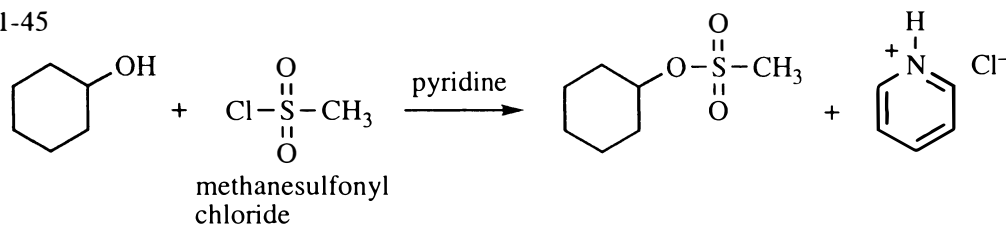


Note that (d), (e), and (f), produce the same alkene.

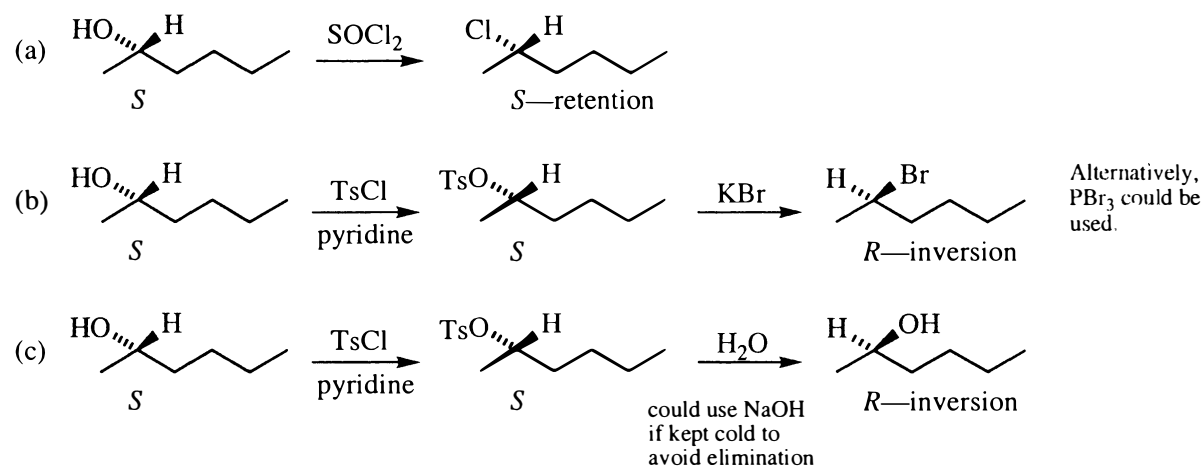
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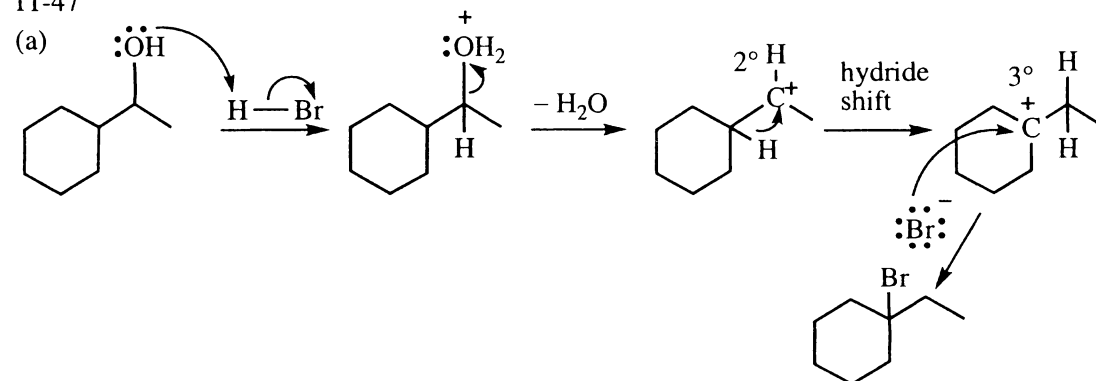
11-45



11-46

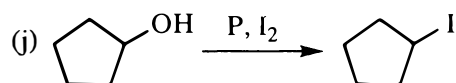
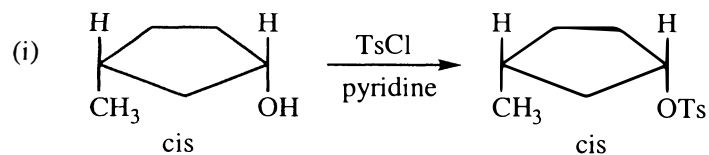
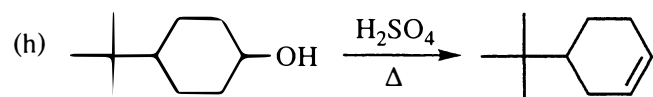
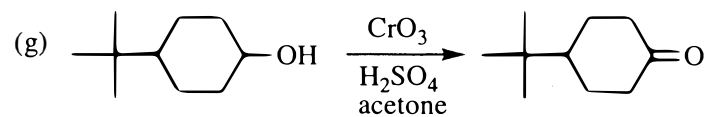
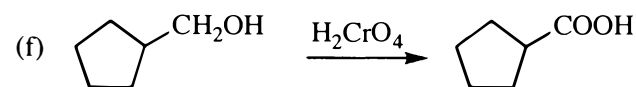
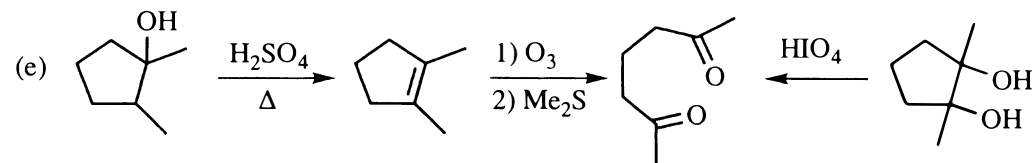
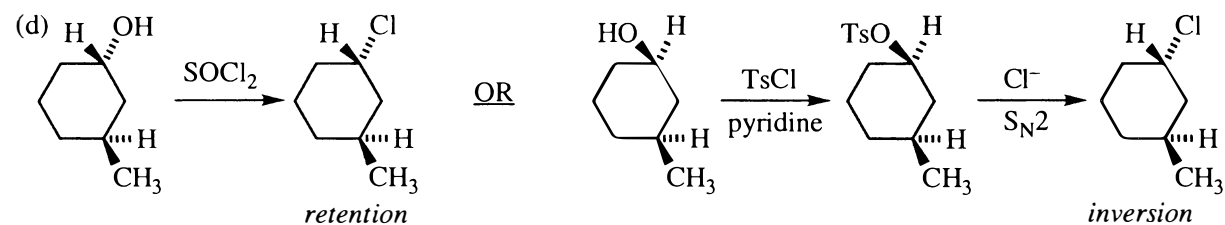
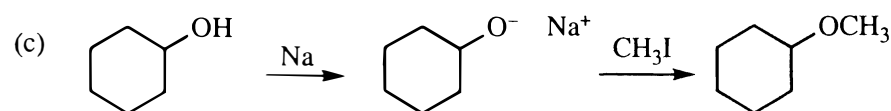
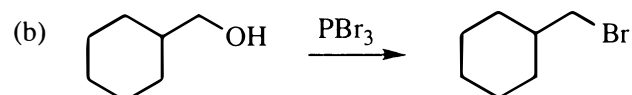
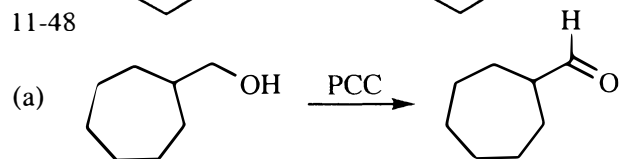
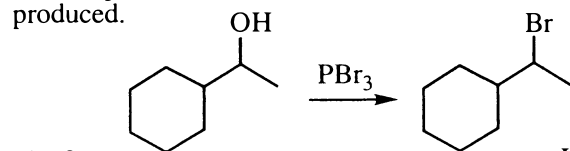


11-47

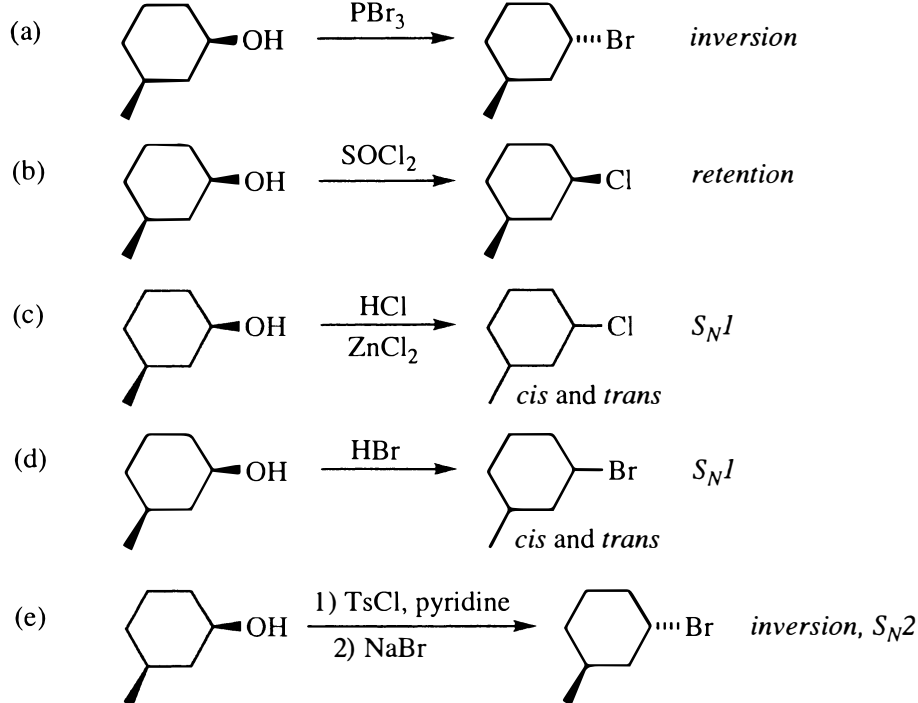


11-47 continued

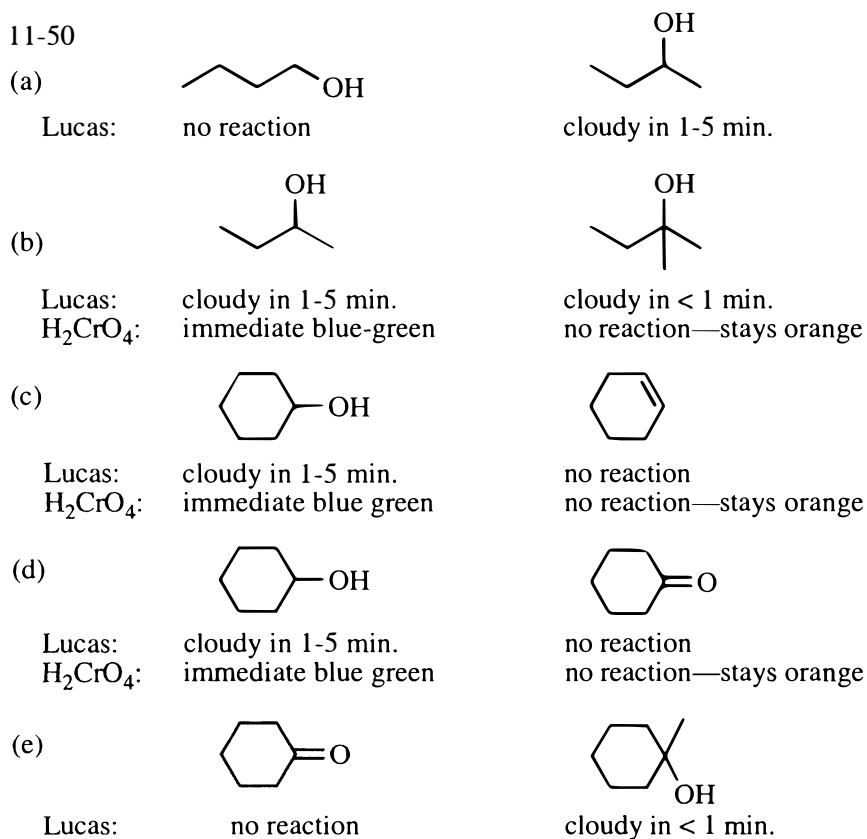
(b) PBr_3 converts alcohols to bromides without rearrangement because no carbocation intermediate is produced.



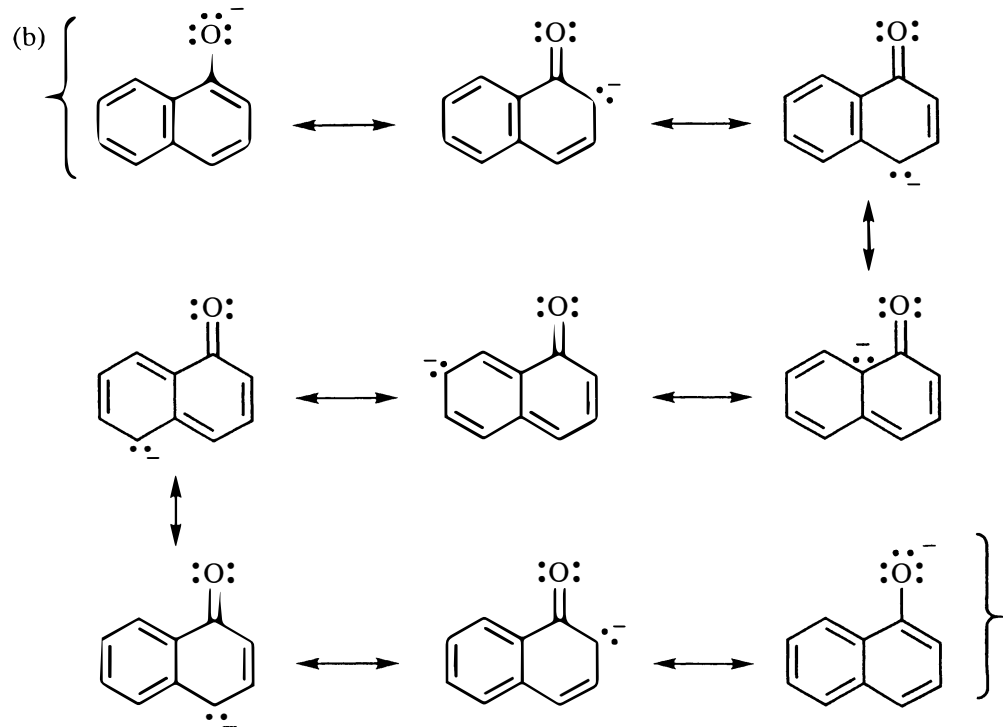
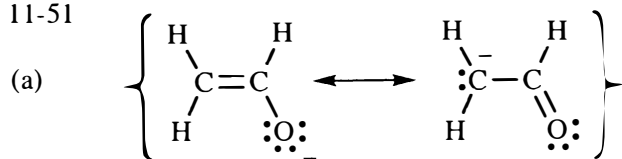
11-49



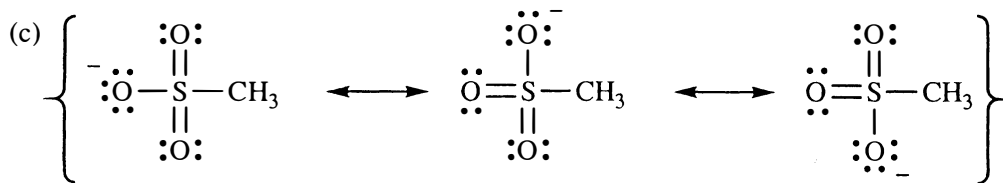
11-50



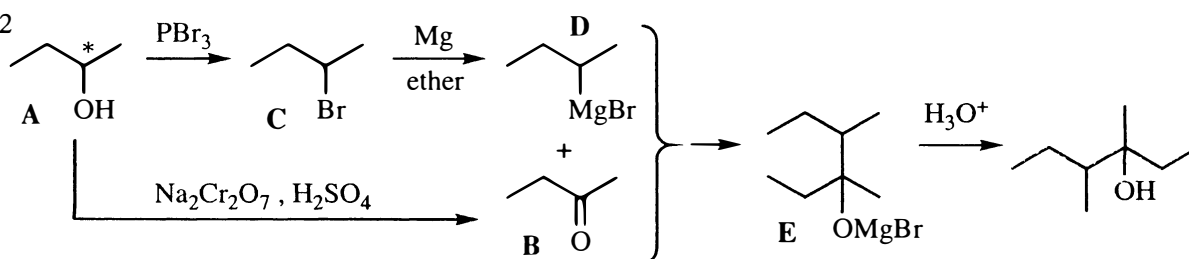
11-51

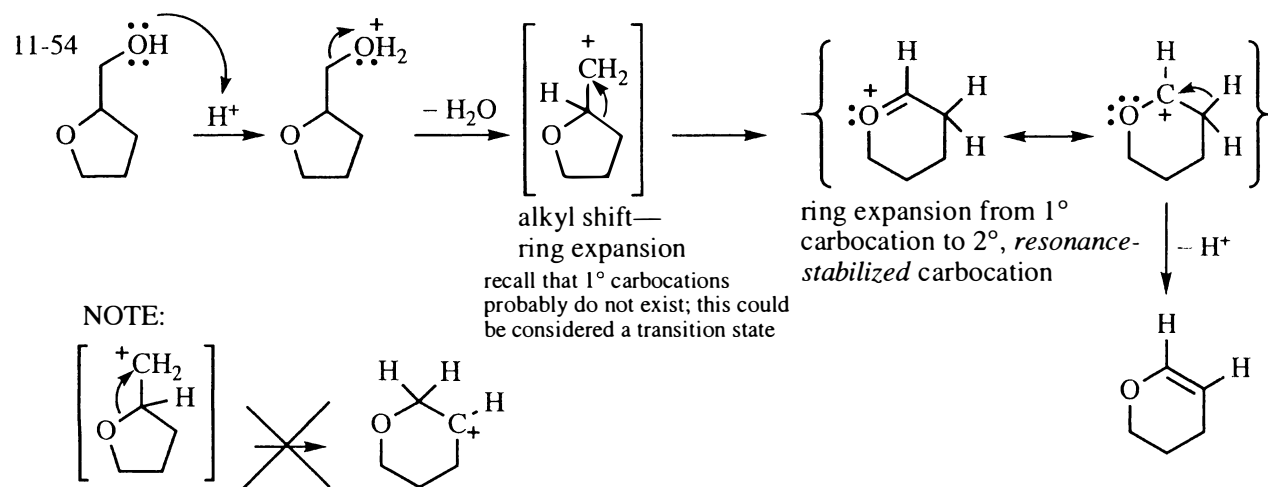
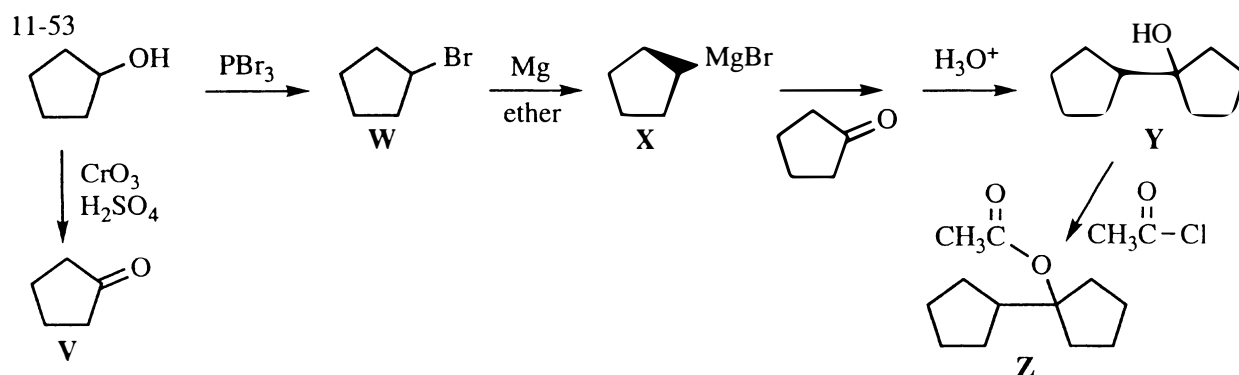


The last three resonance forms are similar to the first three; the change is that the electrons are shown in alternate positions in the benzene ring. To be rigorously correct, these three resonance forms should be included, but most chemists would not write them since they do not reveal extra charge delocalization; understand that they would still be significant, even if not written with the others.



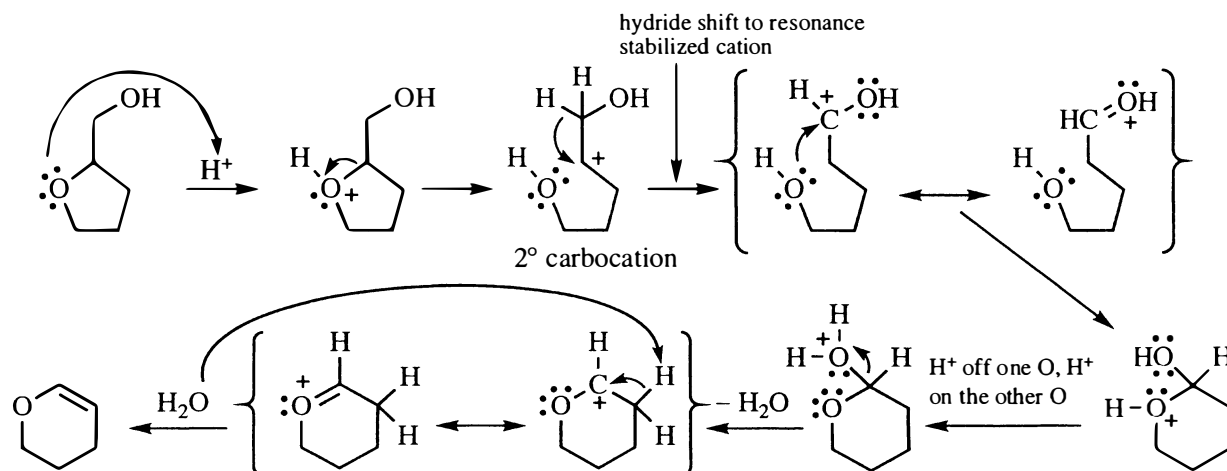
11-52



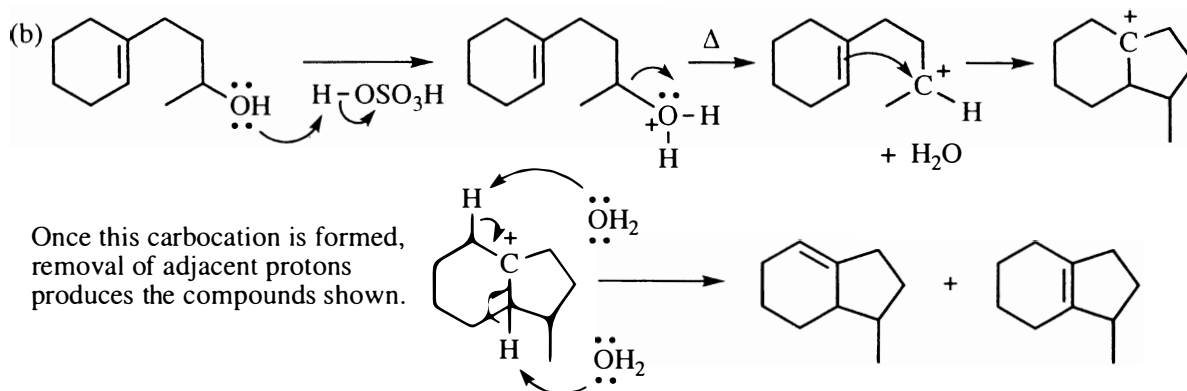
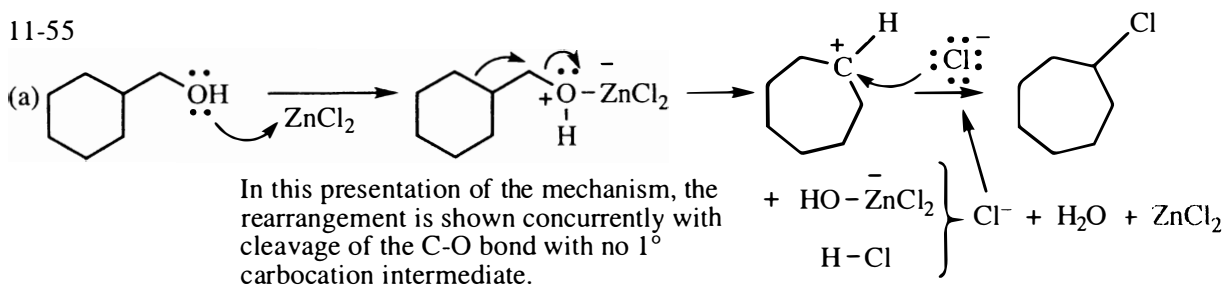


The migration directly above does NOT occur
as the cation produced is not resonance-stabilized.

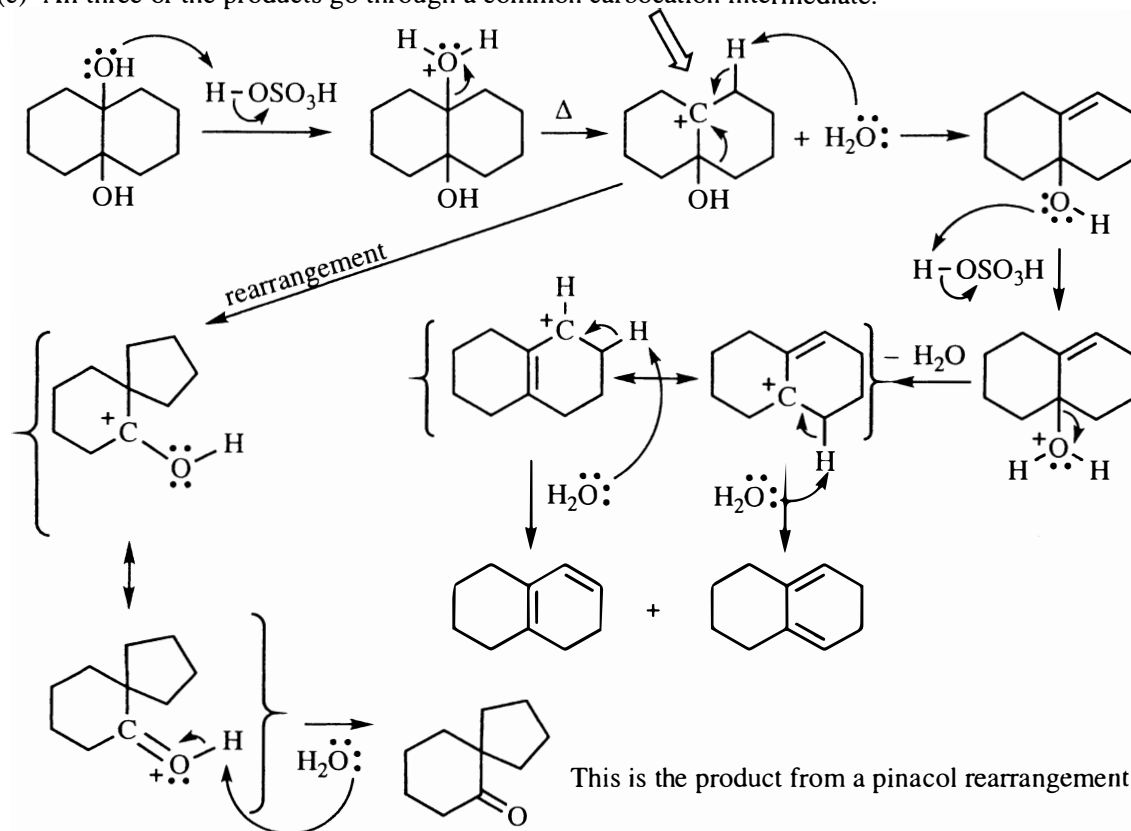
An alternative mechanism could be proposed: protonate the ring oxygen, open the ring to a 2° carbocation followed by a hydride shift to a resonance-stabilized cation, ring closure, and dehydration.



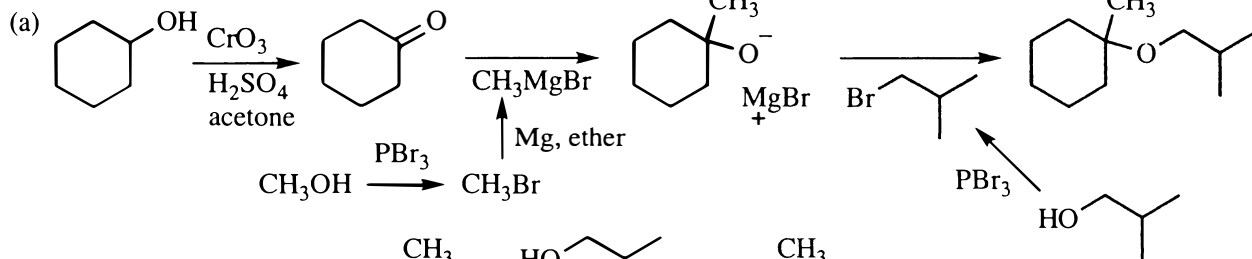
11-55



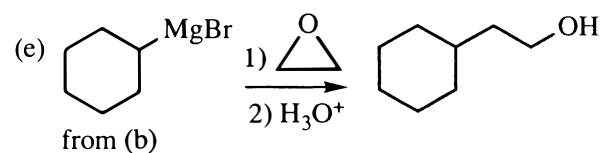
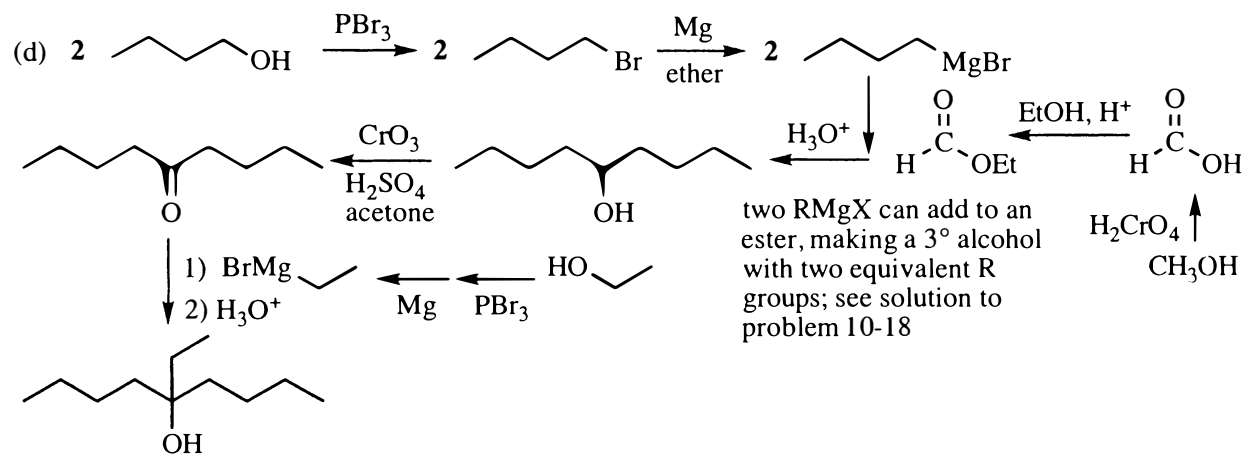
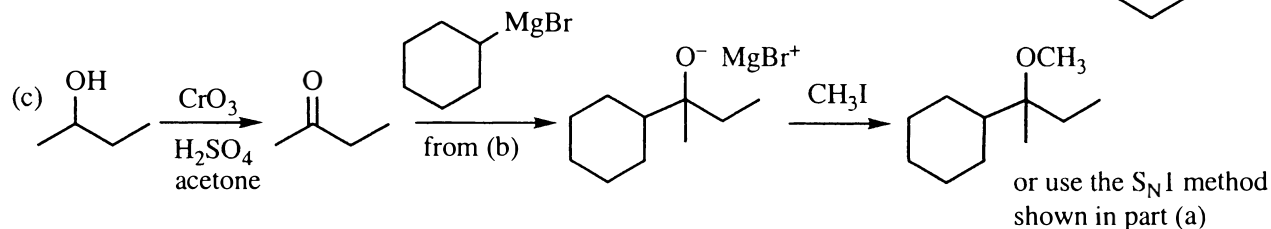
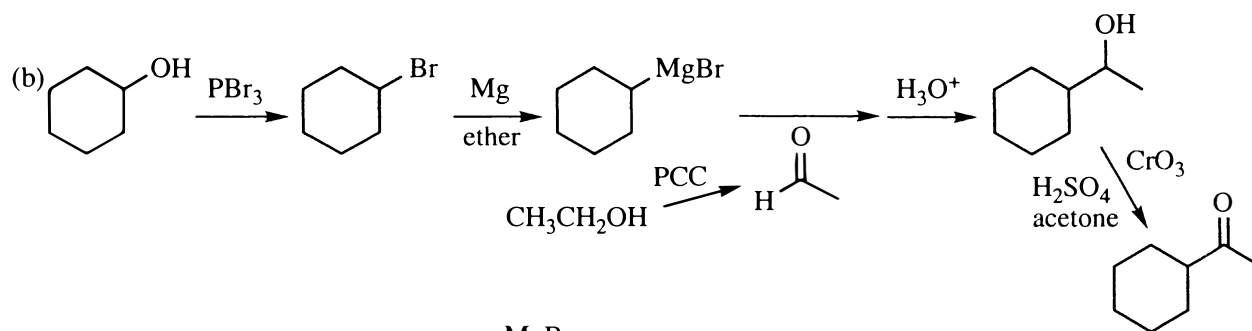
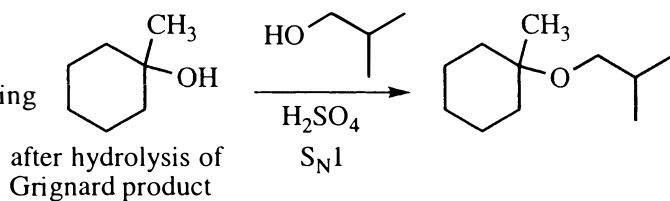
(c) All three of the products go through a common carbocation intermediate.



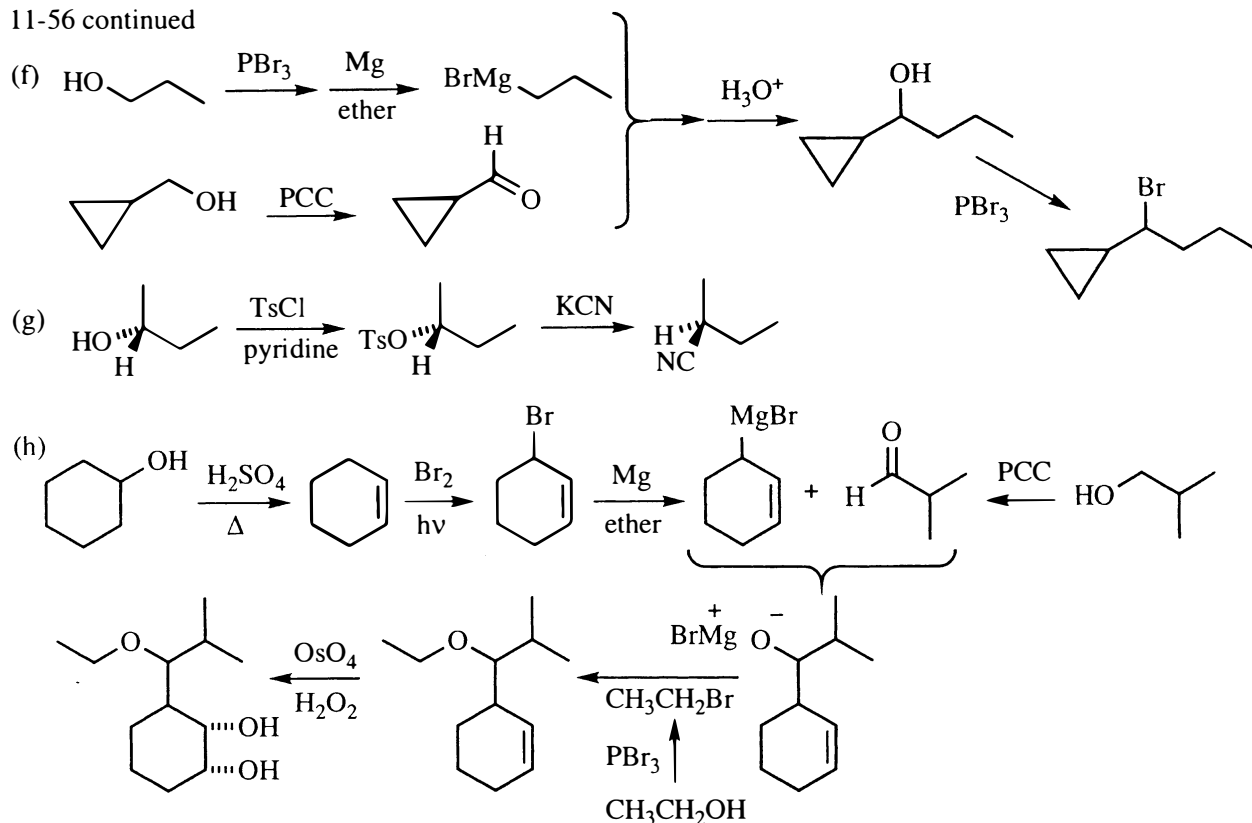
11-56



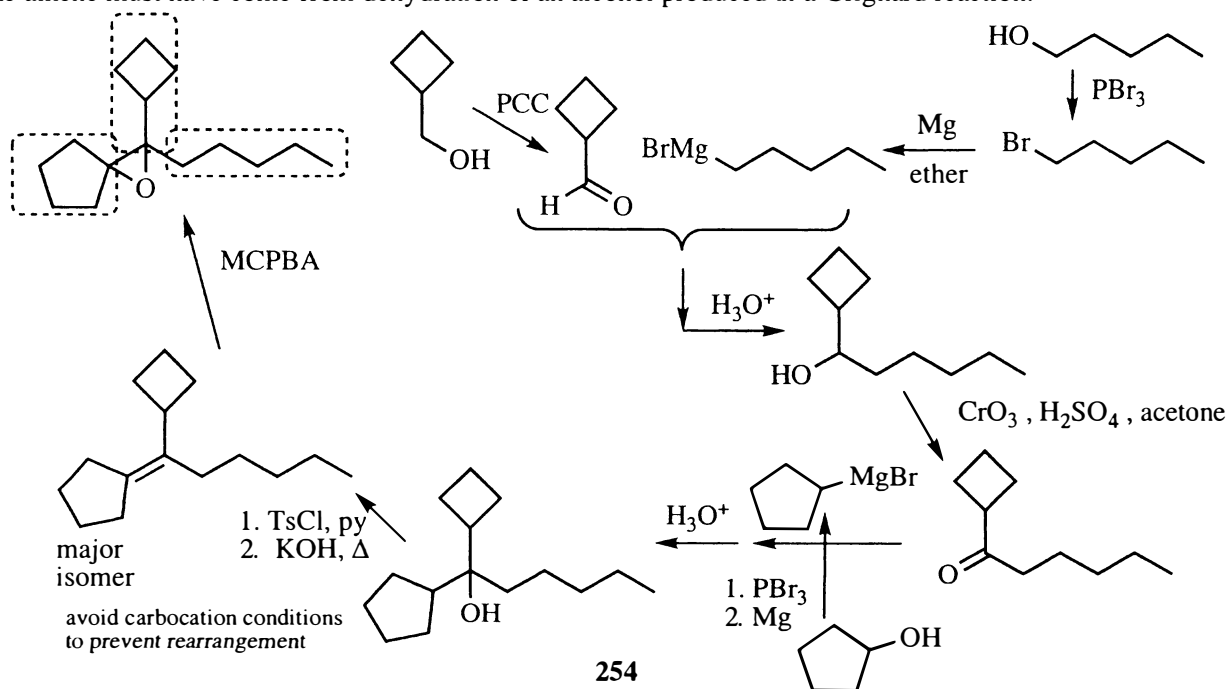
OR: alternative ending



11-56 continued



11-57 For a complicated synthesis like this, begin by working backwards. Try to figure out where the carbon framework came from; in this problem we are restricted to alcohols containing five or fewer carbons. The dashed boxes show the fragments that must be assembled. The most practical way of forming carbon-carbon bonds is by Grignard reactions. The epoxide must be formed from an alkene, and the alkene must have come from dehydration of an alcohol produced in a Grignard reaction.

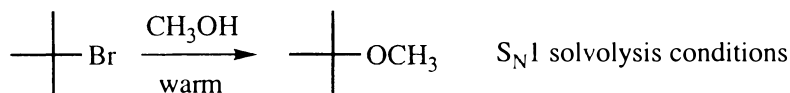


11-58

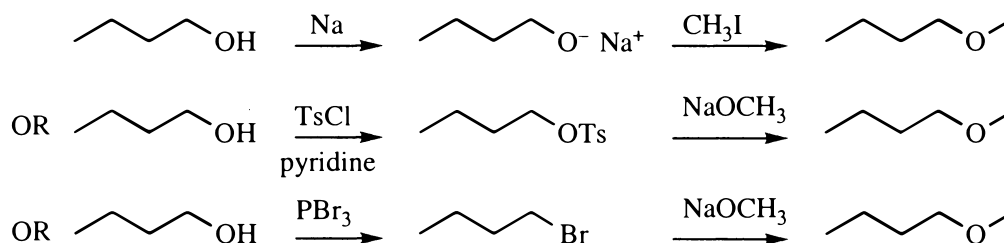
(a) Both of these pseudo-syntheses suffer from the misconception that incompatible reagents or conditions can co-exist. In the first example, the S_N1 conditions of ionization cannot exist with the S_N2 conditions of sodium methoxide. The tertiary carbocation in the first step would not wait around long enough for the sodium methoxide to be added in the second step. (The irony is that the first step by itself, the solvolysis of *t*-butyl bromide in methanol, would give the desired product without the sodium methoxide.)

In the second reaction, the acidic conditions of the first step in which the alcohol is protonated are incompatible with the basic conditions of the second step. If basic sodium methoxide were added to the sulfuric acid solution, the instantaneous acid-base neutralization would give methanol, sodium sulfate, and the starting alcohol. No reaction on the alcohol would occur.

(b)



Several synthetic sequences are possible for the second synthesis.



11-59

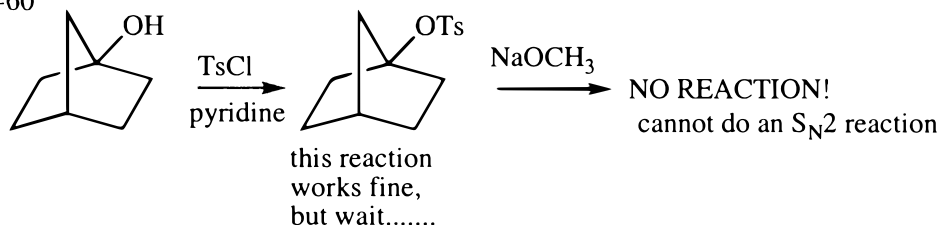
Compound X : —must be a 1° or 2° alcohol with an alkene; no reaction with Lucas leads to a 1° alcohol; can't be allylic as this would give a positive Lucas test



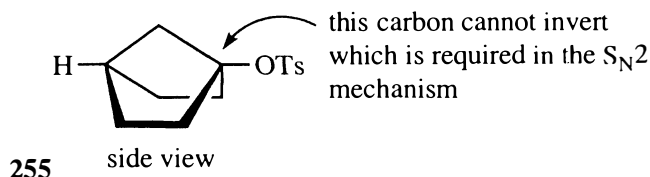
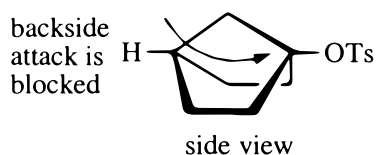
Compound Y : —must be a cyclic ether, not an alcohol and not an alkene; other isomers of cyclic ethers possible



11-60

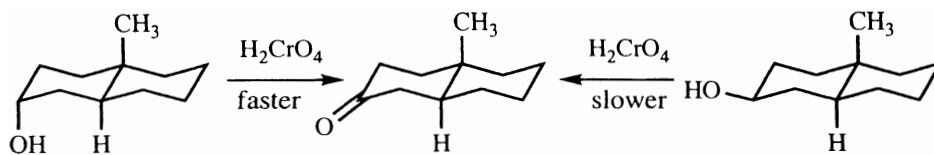


The Williamson ether synthesis is an S_N2 displacement of a leaving group by an alkoxide ion. There are two reasons why this tosylate cannot undergo an S_N2 reaction. First, backside attack cannot occur because the back side of the bridgehead carbon is blocked by the other bridgehead. Second, the bridgehead carbon cannot undergo inversion because of the constraints of the bridged ring system.

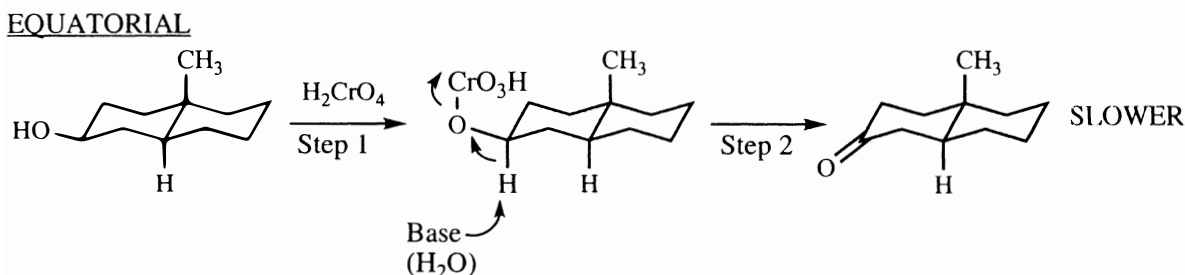
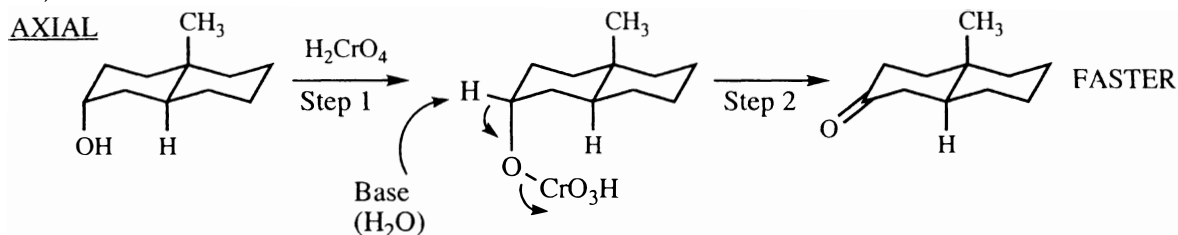


11-61 Let's begin by considering the facts.

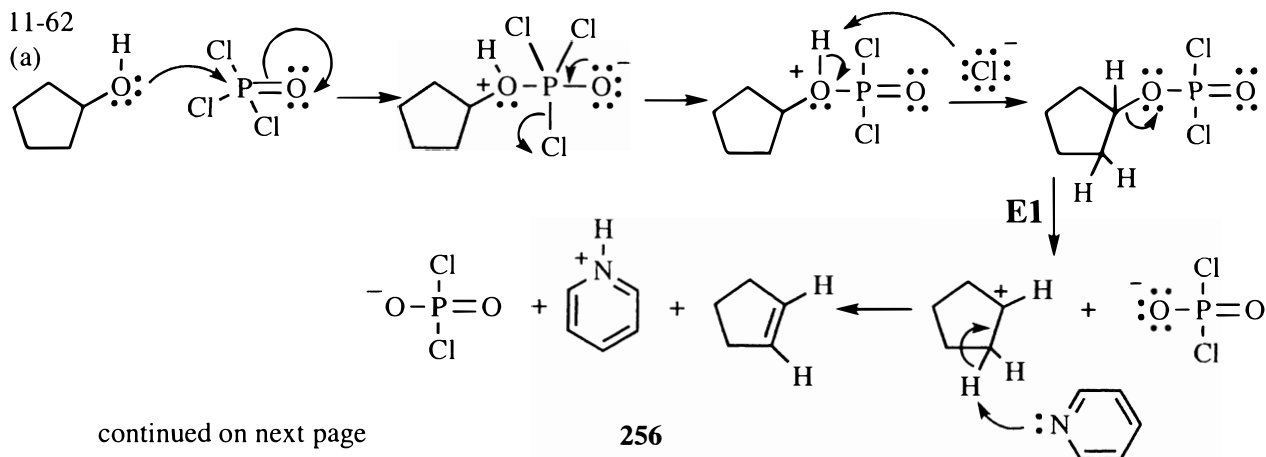
The axial alcohol is oxidized ten times as fast as the equatorial alcohol. (In the olden days, this observation was used as evidence suggesting the stereochemistry of a ring alcohol.)



Second, it is known that the oxidation occurs in two steps: 1) formation of the chromate ester; and 2) loss of H and chromate to form the $\text{C}=\text{O}$. Let's look at each mechanism.

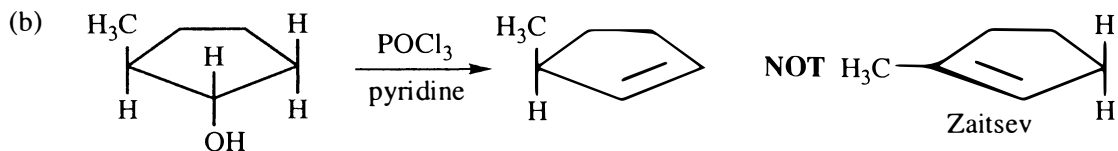
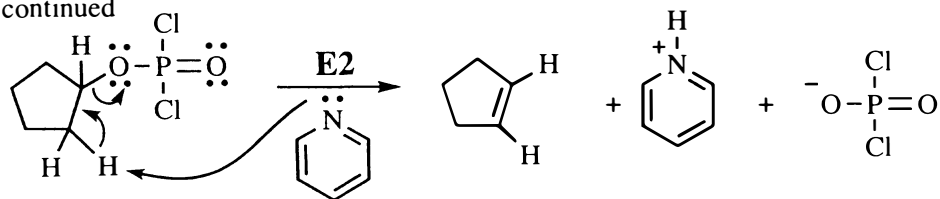


So what do we know about these systems? We know that substituents are more stable in the equatorial position than in the axial position because any group at the axial position has 1,3-diaxial interactions. So what if Step 1 were the rate-limiting step? We would expect that the equatorial chromate ester would form faster than the axial chromate ester; since this is contrary to what the data show, Step 1 is not likely to be rate-limiting. How about Step 2? If the elimination is rate limiting, we would expect the approach of the base (probably water) to the equatorial hydrogen (axial chromate ester) would be faster than the approach of the base to the axial hydrogen (equatorial chromate ester). Moreover, the axial ester is more motivated to leave due to steric congestion associated with such a large group. This is consistent with the relative rates of reaction from experiment. Thus, it is reasonable to conclude that the second step of the mechanism is rate-limiting.



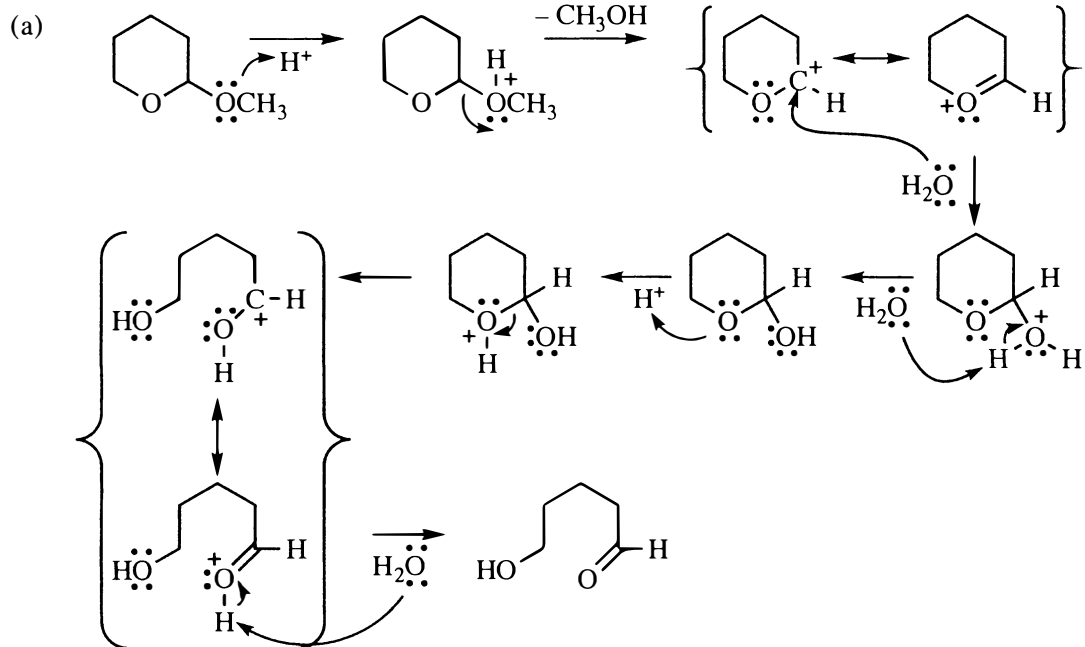
continued on next page

11-62 (a) continued



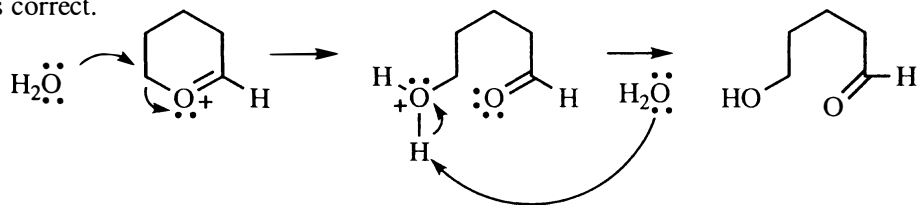
There must be a stereochemical requirement in this elimination. If the Saytzeff alkene is not produced because the methyl group is *trans* to the leaving group, then the H and the leaving group must be *trans* and the elimination must be anti—the characteristic stereochemistry of E2 elimination. This evidence differentiates between the two possibilities in part (a).

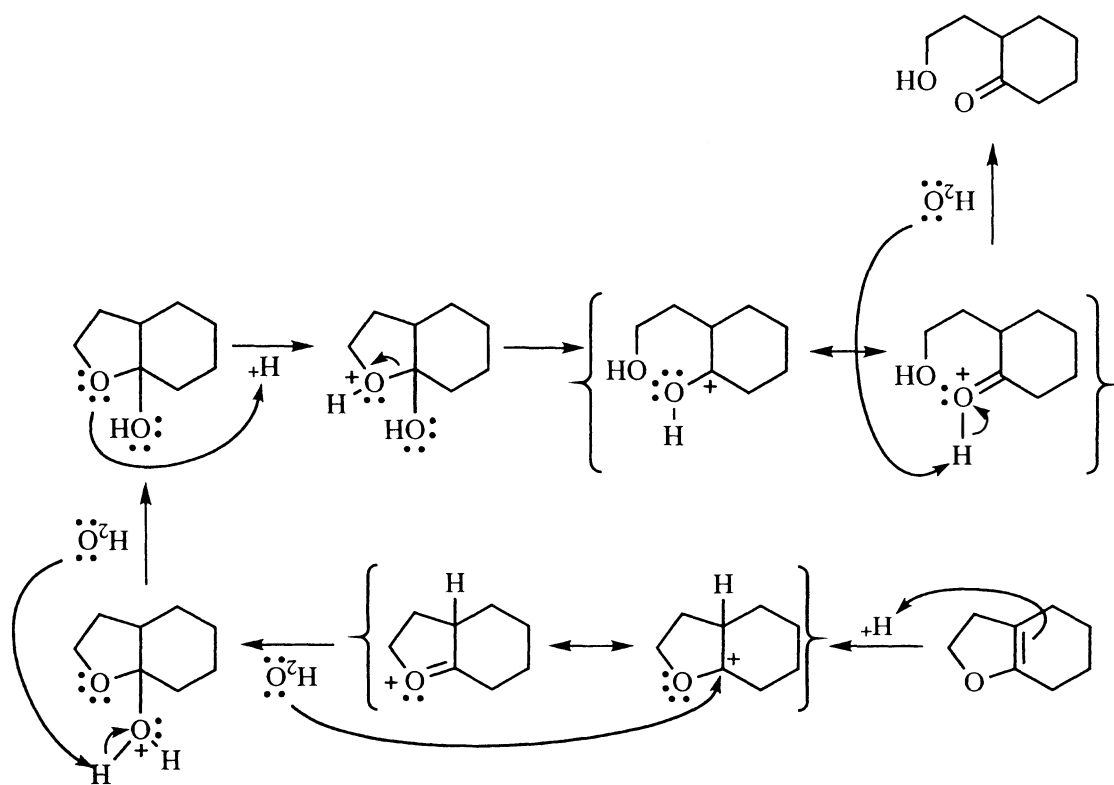
11-63



It is equally likely for protonation to occur first on the ring oxygen, followed by ring opening, then replacement of OCH_3 by water.

Dr. Kantorowski suggests this alternative. He and I will arm wrestle to determine which mechanism is correct.





11-63 continued
(q)

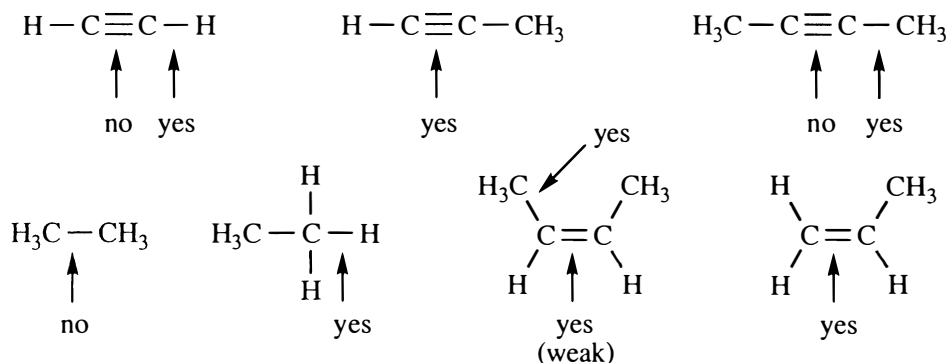
CHAPTER 12—INFRARED SPECTROSCOPY AND MASS SPECTROMETRY

See p. 270 for some useful web sites with infrared and mass spectra.

12-1 The table is completed by recognizing that: $(\bar{\nu})(\lambda) = 10,000$

$\bar{\nu}$ (cm ⁻¹)	4000	3300	3003	2198	1700	1640	1600	400
λ (μm)	2.50	3.03	3.33	4.55	5.88	6.10	6.25	25.0

12-2 In general, only bonds with dipole moments will have an IR absorption.



12-3

(a) alkene: C=C at 1640 cm⁻¹, =C—H at 3080 cm⁻¹

(b) alkane: no peaks indicating sp or sp² carbons present

(c) This IR shows more than one group. There is a terminal alkyne shown by: C≡C at 2100 cm⁻¹, ≡C—H at 3300 cm⁻¹. These signals indicate an aromatic hydrocarbon as well: =C—H at 3050 cm⁻¹, C=C at 1600 cm⁻¹.

12-4

(a) 2° amine, R—NH—R: one peak at 3300 cm⁻¹ indicates an N—H bond; this spectrum also shows a C=C at 1640 cm⁻¹

(b) carboxylic acid: the extremely broad absorption in the 2500-3500 cm⁻¹ range, with a "shoulder" around 2500-2700 cm⁻¹, and a C=O at 1710 cm⁻¹, are compelling evidence for a carboxylic acid

(c) alcohol: strong, broad O—H at 3330 cm⁻¹

12-5

(a) conjugated ketone: the small peak at 3030 cm⁻¹ suggests =C—H, and the strong peak at 1685 cm⁻¹ is consistent with a ketone conjugated with the alkene. The C=C is indicated by a very small peak around 1600 cm⁻¹.

(b) ester: the C=O absorption at 1738 cm⁻¹ (higher than the ketone's 1710 cm⁻¹), in conjunction with the strong C—O at 1200 cm⁻¹, points to an ester

(c) amide: the two peaks at 3160-3360 cm⁻¹ are likely to be an NH₂ group; the strong peak at 1640 cm⁻¹ is too strong for an alkene, so it must be a different type of C=X, in this case a C=O, so low because it is part of an amide

12-6

(a) The small peak at 1642 cm⁻¹ indicates a C=C, consistent with the =C—H at 3080 cm⁻¹. This appears to be a simple alkene.

(b) The strong absorption at 1691 cm⁻¹ is unmistakably a C=O. The smaller peak at 1626 cm⁻¹ indicates a C=C, probably conjugated with the C=O. The two peaks at 2712 cm⁻¹ and at 2814 cm⁻¹ represent H—C=O confirming that this is an aldehyde.

12-6 continued

(c) The strong peak at 1650 cm^{-1} is $\text{C}=\text{C}$, probably conjugated as it is unusually strong. The 1703 cm^{-1} peak appears to be a conjugated $\text{C}=\text{O}$, undeniably a carboxylic acid because of the strong, broad $\text{O}-\text{H}$ absorption from $2400\text{--}3400\text{ cm}^{-1}$.

(d) The $\text{C}=\text{O}$ absorption at 1742 cm^{-1} coupled with $\text{C}-\text{O}$ at 1220 cm^{-1} suggest an ester. The small peak at 1604 cm^{-1} , peaks above 3000 cm^{-1} , and peaks in the $600\text{--}800\text{ cm}^{-1}$ region indicate a benzene ring.

12-7

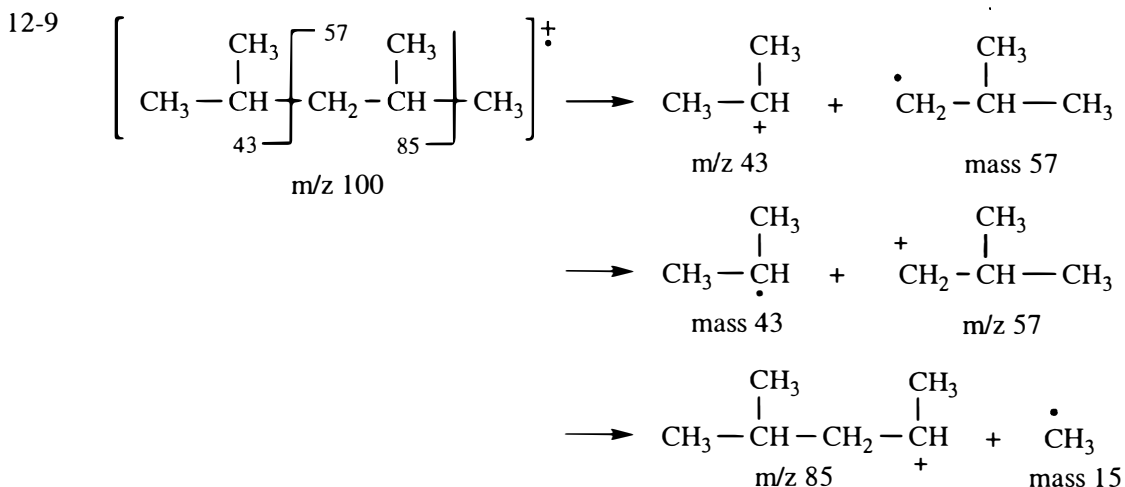
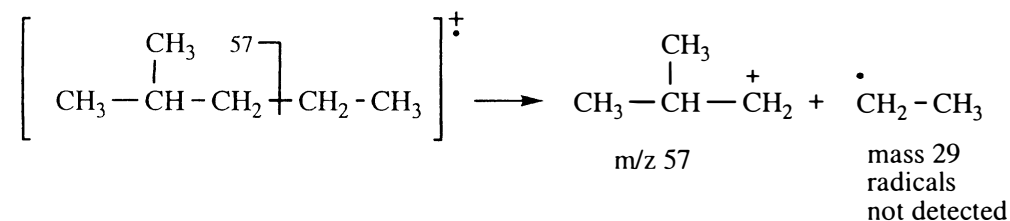
(a) The M and $M+2$ peaks of equal intensity identify the presence of bromine. The mass of M (156) minus the weight of the lighter isotope of bromine (79) gives the mass of the rest of the molecule: $156 - 79 = 77$. The C_6H_5 (phenyl) group weighs 77; this compound is bromobenzene, $\text{C}_6\text{H}_5\text{Br}$.

(b) The m/z 127 peak shows that iodine is present. The molecular ion minus iodine gives the remainder of the molecule: $156 - 127 = 29$. The C_2H_5 (ethyl) group weighs 29; this compound is iodoethane, $\text{C}_2\text{H}_5\text{I}$.

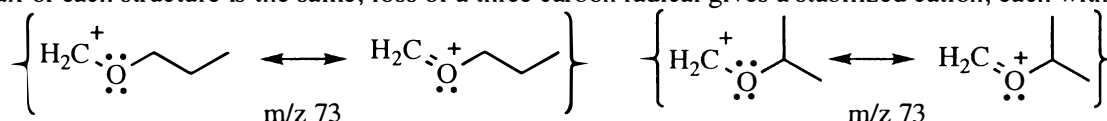
(c) The M and $M+2$ peaks have relative intensities of about 3:1, a sure sign of chlorine. The mass of M minus the mass of the lighter isotope of chlorine gives the mass of the remainder of the molecule: $90 - 35 = 55$. A fragment of mass 55 is not one of the common alkyl groups (15, 29, 43, 57, *etc.*, increasing in increments of 14 mass units (CH_2)), so the presence of an atom like oxygen must be considered. In addition to the chlorine atom, mass 55 could be C_4H_7 or $\text{C}_3\text{H}_3\text{O}$. Possible molecular formulas are $\text{C}_4\text{H}_7\text{Cl}$ or $\text{C}_3\text{H}_3\text{ClO}$.

(d) The odd-mass molecular ion indicates the presence of an odd number of nitrogen atoms (always begin by assuming *one* nitrogen). The rest of the molecule must be: $115 - 14 = 101$; this is most likely C_7H_{17} . The formula $\text{C}_7\text{H}_{17}\text{N}$ is the correct formula of a molecule with no elements of unsaturation. The seven carbons probably include alkyl groups like ethyl or propyl or isopropyl.

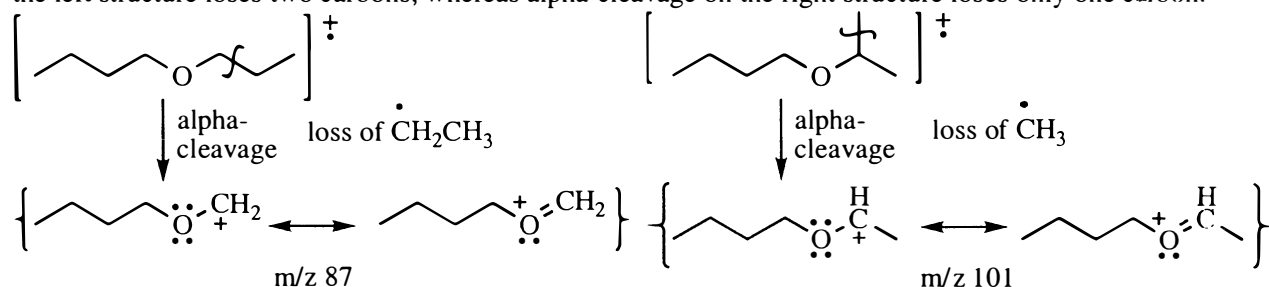
12-8 Recall that radicals are not detected in mass spectrometry; only positively-charged ions are detected.



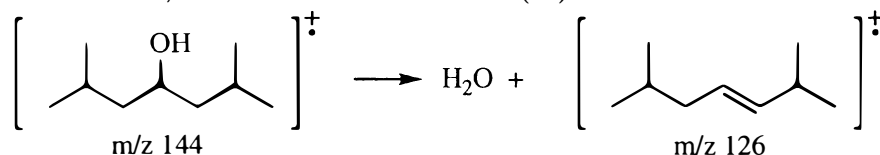
12-10 The molecular weight of each isomer is 116 g/mole, so the molecular ion appears at m/z 116. The left half of each structure is the same; loss of a three carbon radical gives a stabilized cation, each with m/z 73:



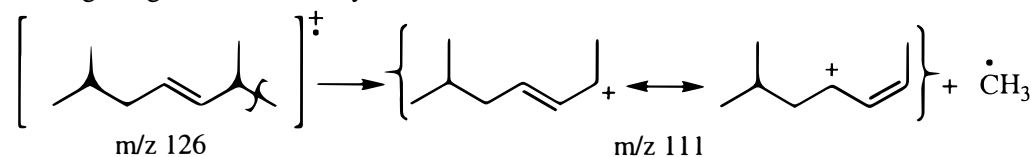
Where the two structures differ is in the alpha-cleavage on the right side of the oxygen. Alpha-cleavage on the left structure loses two carbons, whereas alpha-cleavage on the right structure loses only one carbon.



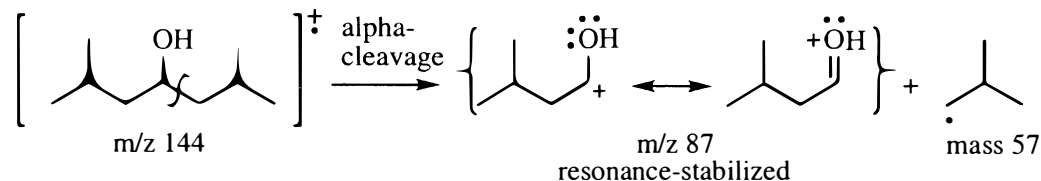
12-11 2,6-Dimethylheptan-4-ol, $\text{C}_9\text{H}_{20}\text{O}$, has molecular weight 144. The highest mass peak at 126 is *not* the molecular ion, but rather is the loss of water (18) from the molecular ion.



The peak at m/z 111 is loss of another 15 (CH_3) from the fragment of m/z 126. This is called allylic cleavage; it generates a 2° , allylic, resonance-stabilized carbocation.



The peak at m/z 87 results from fragmentation on one side of the alcohol:

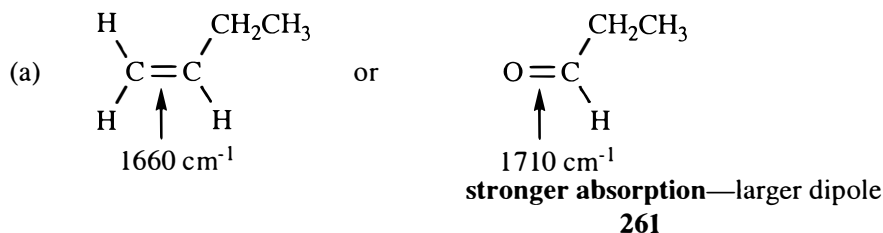


12-12 Please refer to solution 1-20, page 12 of this Solutions Manual.

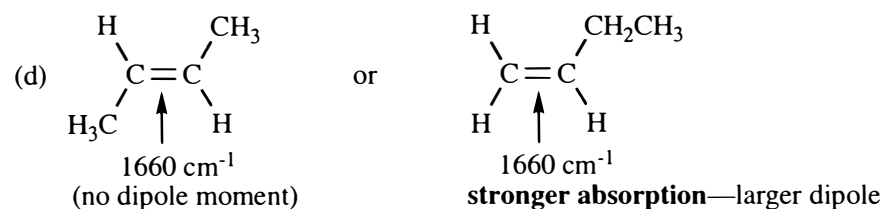
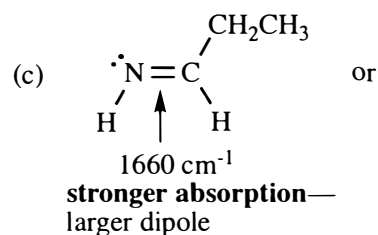
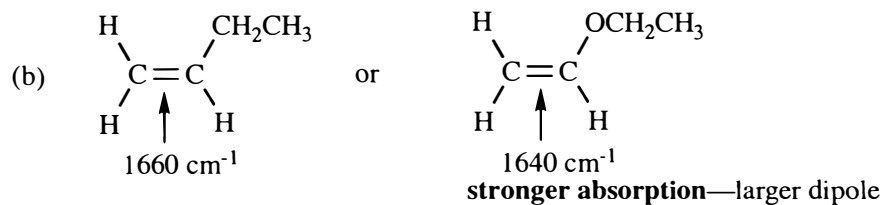
12-13 Divide the numbers into 10,000 to arrive at the answer.

(a) 1603 cm^{-1} (b) 2959 cm^{-1} (c) 1709 cm^{-1} (d) 1739 cm^{-1} (e) 2212 cm^{-1} (f) 3300 cm^{-1}

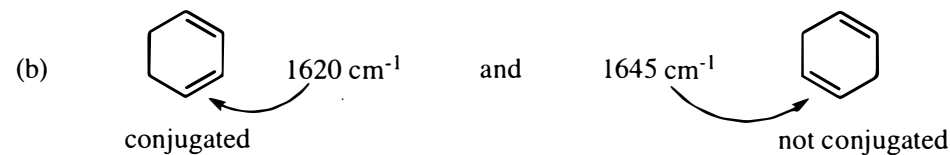
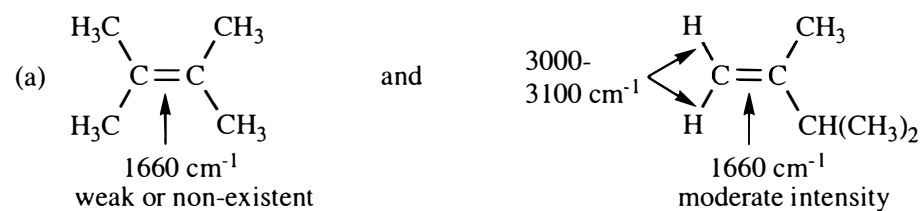
12-14



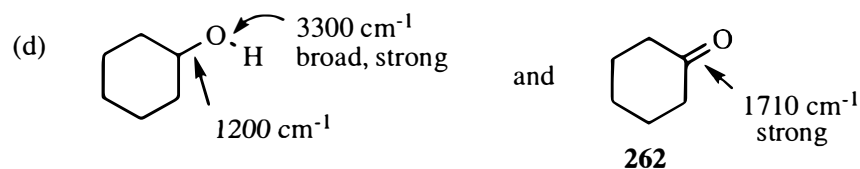
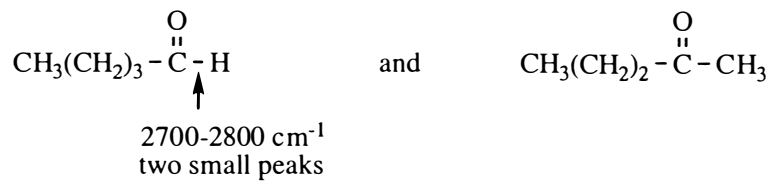
12-14 continued



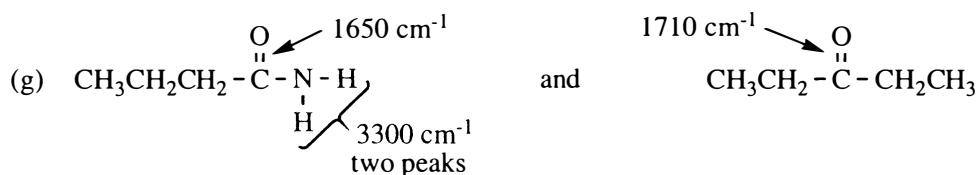
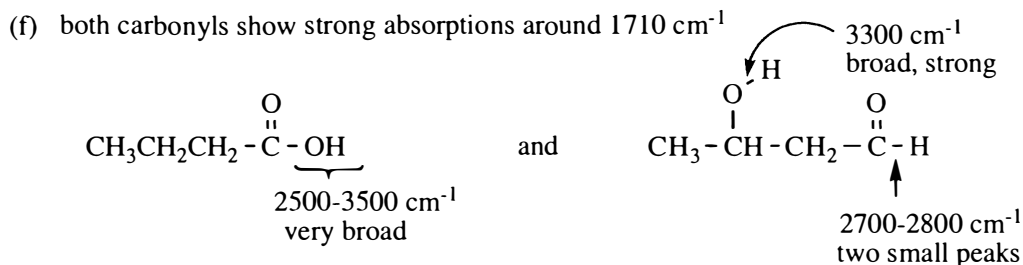
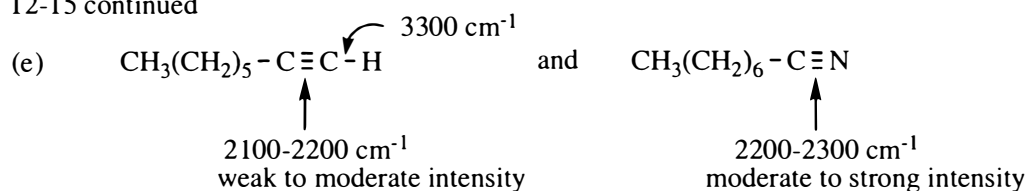
12-15



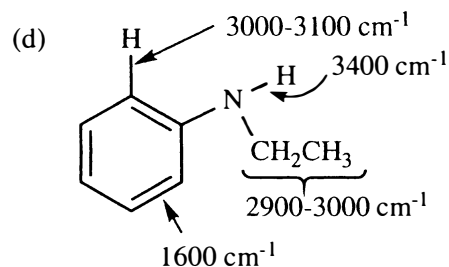
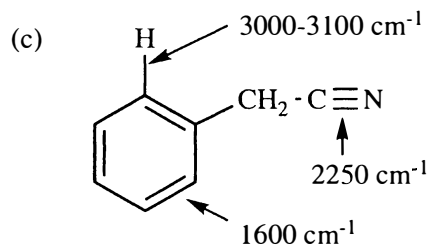
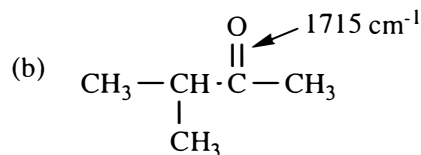
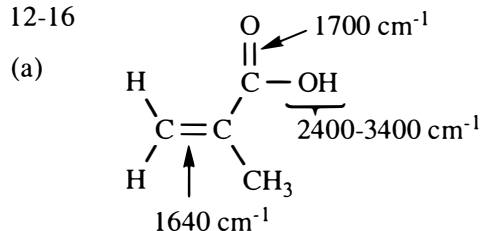
(c) both carbonyls show strong absorptions around 1710 cm⁻¹



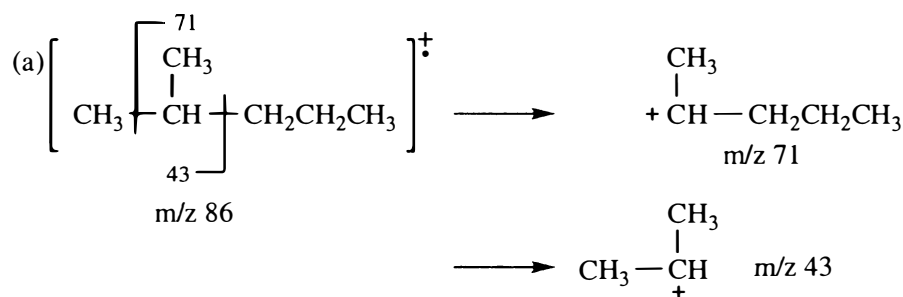
12-15 continued



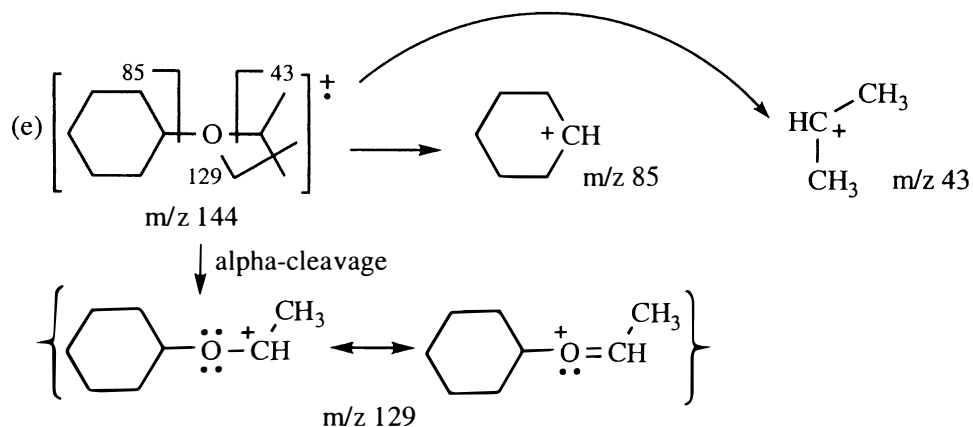
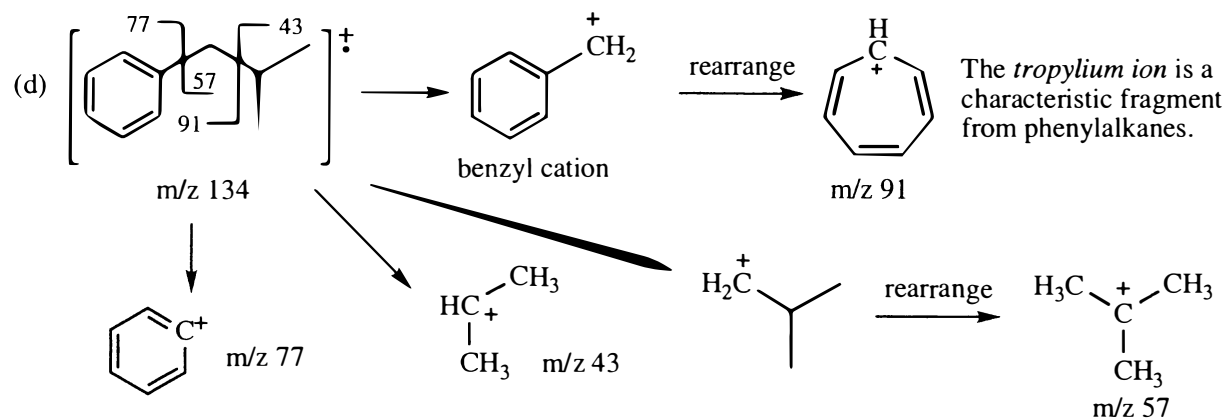
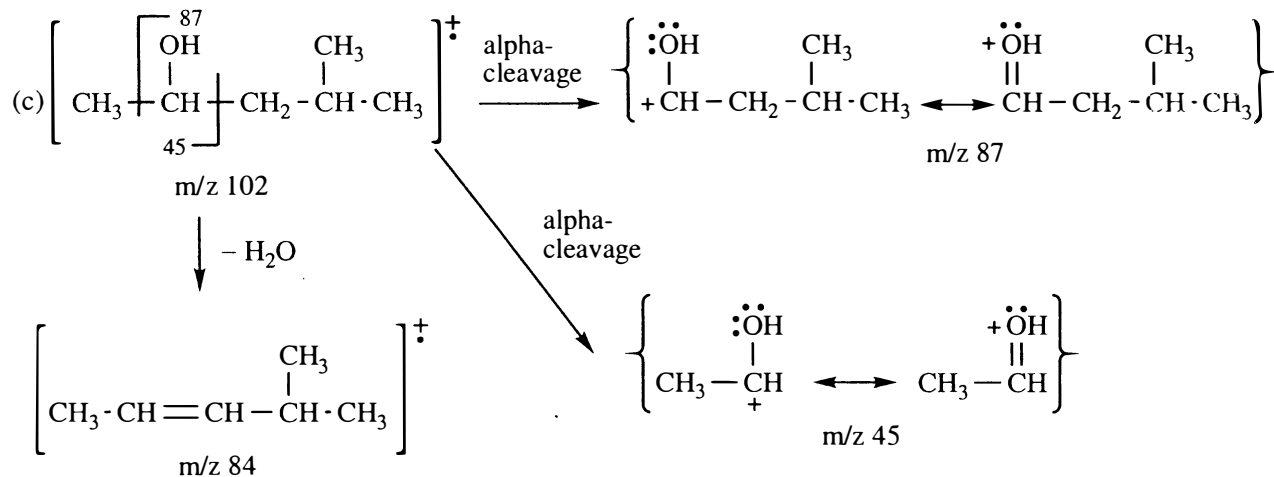
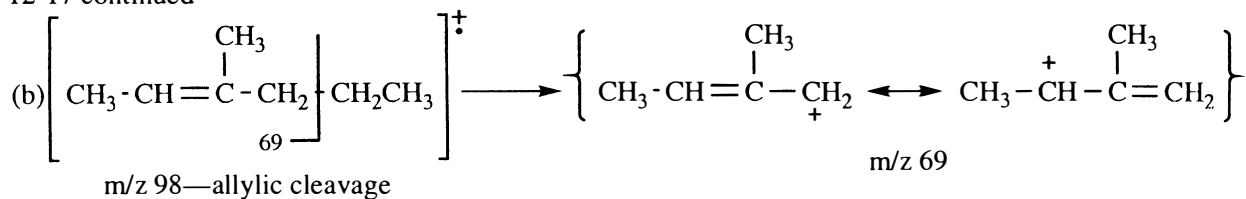
12-16



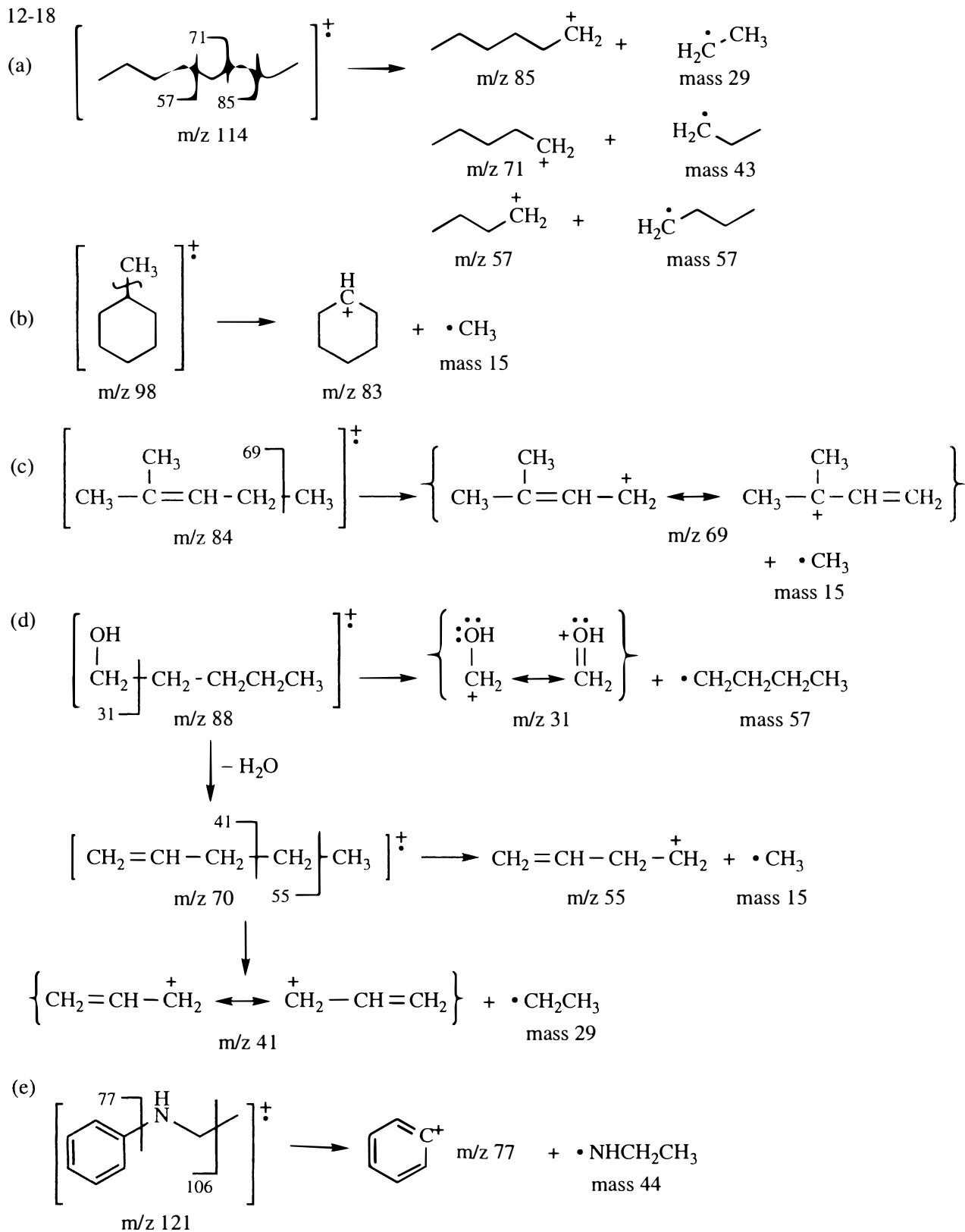
12-17



12-17 continued

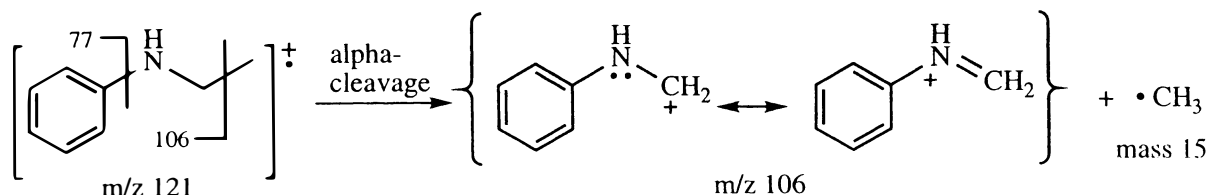


12-18



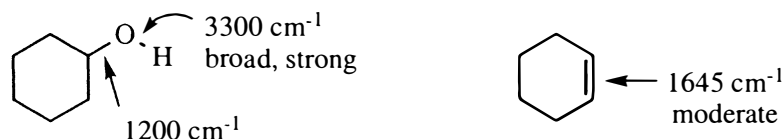
continued on next page

12-18 (e) continued



12-19

(a) The characteristic frequencies of the OH absorption and the C=C absorption will indicate the presence or absence of the groups. A spectrum with an absorption around 3300 cm^{-1} will have some cyclohexanol in it; if that same spectrum also has a peak at 1645 cm^{-1} , then the sample will also contain some cyclohexene. Pure samples will have peaks representative of only one of the compounds and not the other. Note that *quantitation* of the two compounds would be very difficult by IR because the strength of absorptions are very different. Usually, other methods are used in preference to IR for quantitative measurements.

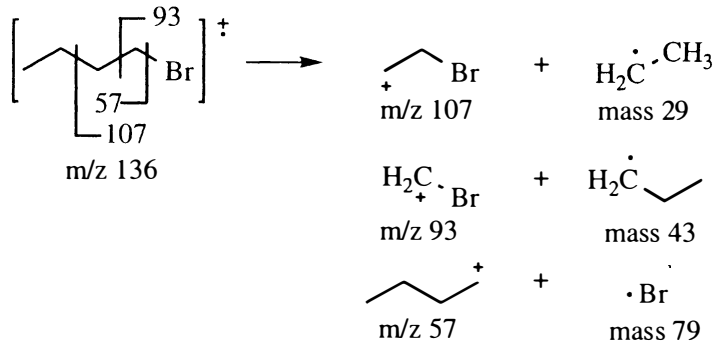


(b) Mass spectrometry can be misleading with alcohols. Usually, alcohols dehydrate in the inlet system of a mass spectrometer, and the characteristic peaks observed in the mass spectrum are those of the alkene, not of the parent alcohol. For this particular analysis, mass spectrometry would be unreliable and perhaps misleading.

12-20

(a) The "student prep" compound must be 1-bromobutane. The most obvious feature of the mass spectrum is the pair of peaks at M and $M+2$ of approximately equal heights, characteristic of a bromine atom. Loss of bromine (79) from the molecular ion at 136 gives a mass of 57, C_4H_9 , a butyl group. Which of the four possible butyl groups? The peaks at 107 (loss of 29, C_2H_5) and 93 (loss of 43, C_3H_7) are consistent with a linear chain, not a branched chain.

(b) The base peak at 57 is so strong because the carbon-halogen bond is the weakest in the molecule. Typically, loss of halogen is the dominant fragmentation in alkyl halides.



12-21

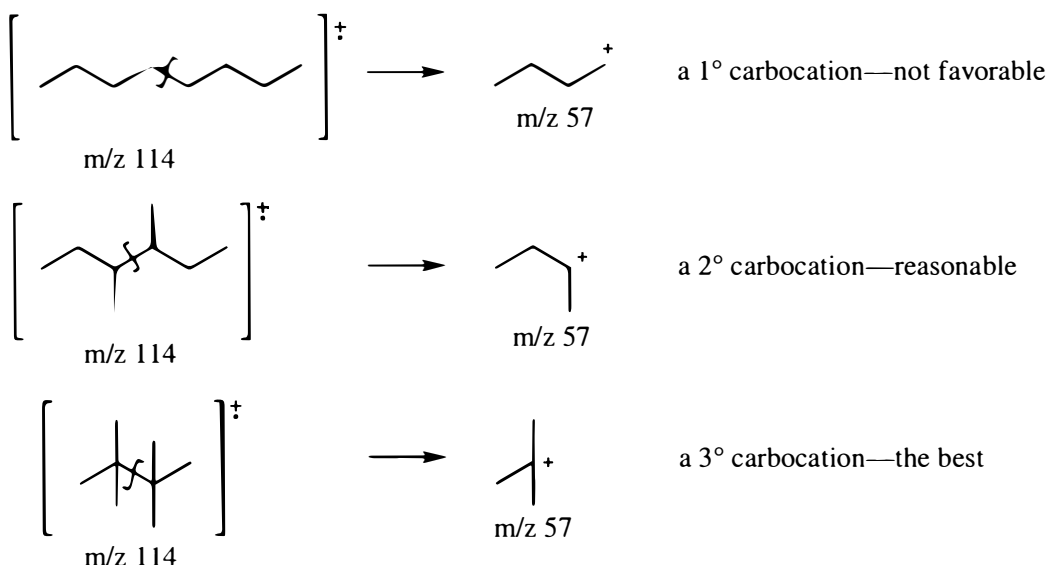
(a) Deuterium has twice the mass of hydrogen, but similar spring constant, k . Compare the frequency of C—D vibration to C—H vibration by setting up a ratio, changing only the mass (substitute $2m$ for m).

$$\frac{\nu_D}{\nu_H} = \frac{\sqrt{k/2m}}{\sqrt{k/m}} = \frac{\sqrt{1/2} \sqrt{k/m}}{\sqrt{k/m}} = \sqrt{1/2} = 0.707$$

$$\nu_D = 0.707 \nu_H = 0.707 (3000 \text{ cm}^{-1}) \approx \mathbf{2100 \text{ cm}^{-1}}$$

(b) The functional group most likely to be confused with a C—D stretch is the alkyne (carbon-carbon triple bond), which appears in the same region and is often very weak.

12-22



The most likely fragmentation of 2,2,3,3-tetramethylbutane will give a 3° carbocation, the most stable of the common alkyl cations. The molecular ion should be small or non-existent while m/z 57 is likely to be the base peak, whereas the molecular ion peaks will be more prominent for *n*-octane and for 3,4-dimethylhexane.

12-23

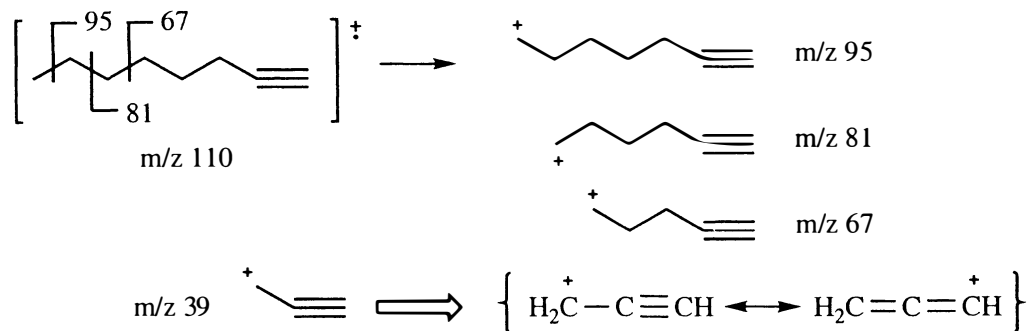
(a) The information that this mystery compound is a hydrocarbon makes interpreting the mass spectrum much easier. (It is relatively simple to tell if a compound has chlorine, bromine, or nitrogen by a mass spectrum, but oxygen is difficult to determine by mass spectrometry alone.) A hydrocarbon with molecular ion of 110 can have only 8 carbons ($8 \times 12 = 96$) and 14 hydrogens. The formula C_8H_{14} has two elements of unsaturation.

(b) The IR will be useful in determining what the elements of unsaturation are. Cycloalkanes are generally not distinguishable in the IR. An alkene should have an absorption around $1600\text{--}1650 \text{ cm}^{-1}$; none is present in this IR. An alkyne should have a small, sharp peak around 2200 cm^{-1} —PRESENT AT 2120 cm^{-1} ! Also, a sharp peak around 3300 cm^{-1} indicates a hydrogen on an alkyne, so the alkyne is at one end of the molecule. Both elements of unsaturation are accounted for by the alkyne.

12-23

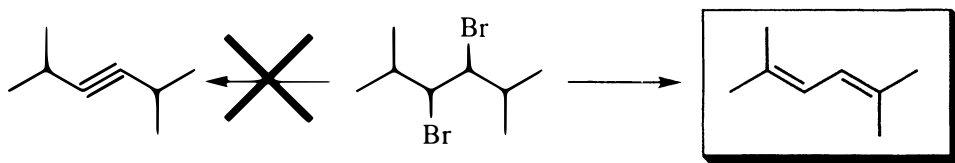
(c) The only question is how are the other carbons arranged. The mass spectrum shows a progression of peaks from the molecular ion at 110 to 95 (loss of CH_3), to 81 (loss of C_2H_5), to 67 (loss of C_3H_7). The mass spectrum suggests it is a linear chain. The extra evidence that hydrogenation of the mystery compound gives *n*-octane verifies that the chain is linear. The original compound must be oct-1-yne.

(d) The base peak is so strong because the ion produced is stabilized by resonance.

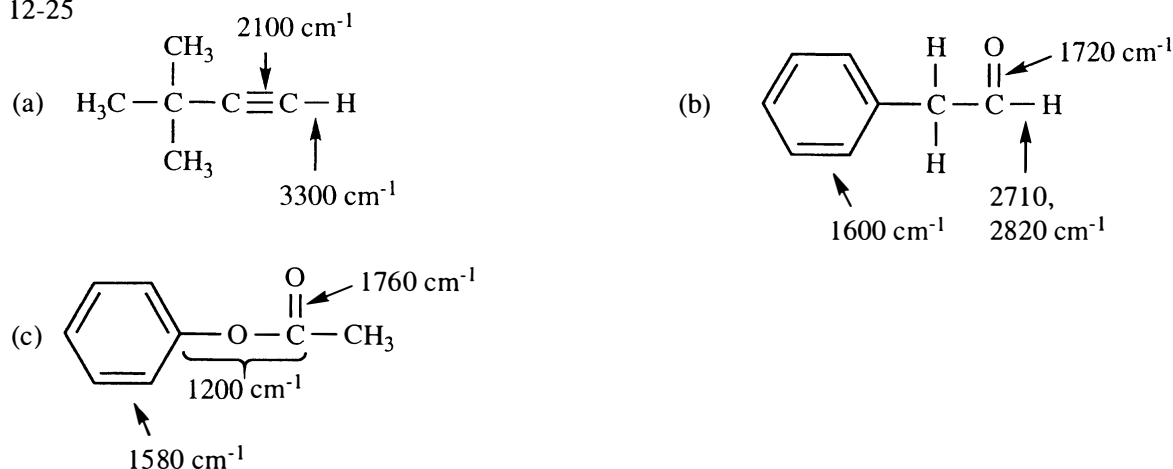


12-24

(a) and (b) The mass spec is consistent with the formula of the alkyne, C_8H_{14} , mass 110. The IR is not consistent with the alkyne, however. Often, symmetrically substituted alkynes have a miniscule $\text{C} \equiv \text{C}$ peak, so the fact that the IR does not show this peak does not prove that the alkyne is absent. The important evidence in the IR is the significant peak at 1620 cm^{-1} ; this absorption is characteristic of a conjugated diene. Instead of the alkyne being formed, the reaction must have been a double elimination to the diene.

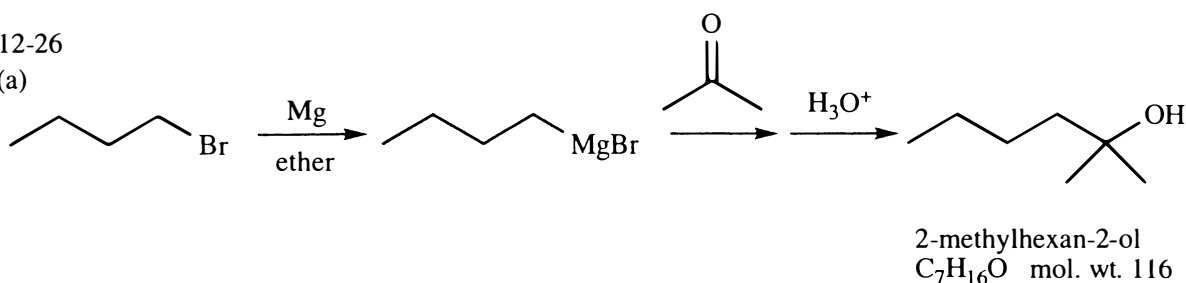


12-25

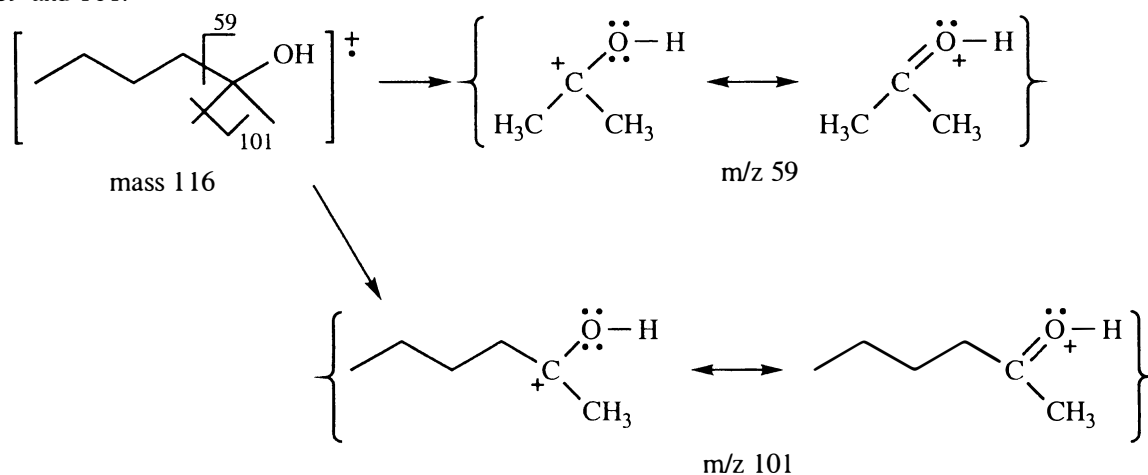


12-26

(a)



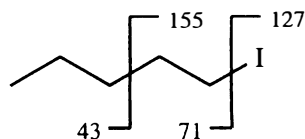
(b) The molecular ion is not visible in the spectrum. Alcohols typically dehydrate in the hot inlet system of the mass spectrometer, especially true for 3° alcohols that are the easiest type to dehydrate. The two fragmentations that produce a resonance-stabilized carbocation give the major peaks in the spectrum at *m/z* 59 and 101.



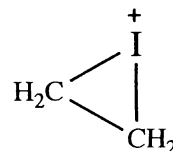
12-27 The unknown compound has peaks in the mass spec at *m/z* 198, 155, 127, 71, and 43. It is helpful that the masses of two of the fragments, 155 and 43, sum to 198, as do the other two fragment masses, 127 and 71. We can say with certainty that the molecular ion is at *m/z* 198, and that the unknown is a relatively simple molecule with two main fragmentations.

This is a fairly high mass for a simple compound; some heavy group must be present. What is NOT present is N because of the even molecular ion mass, nor Cl nor Br because of the lack of isotope peaks, nor a phenyl group because of no peak at 77. The progression of alkyl group masses: 15, 29, **43**, 57, **71**, 85, 99—includes two of the peaks, so it appears that the unknown contains a propyl group and a pentyl group (the propyl could be part of the pentyl group). The 127 fragment is key; the fragment C₉H₁₉ has this mass, but we would expect much more fragmentation from a nine carbon piece. There must be some other explanation for this 127 peak.

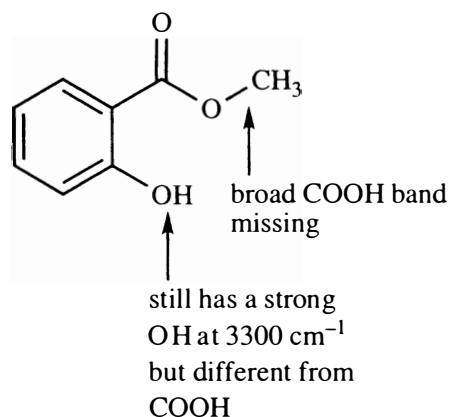
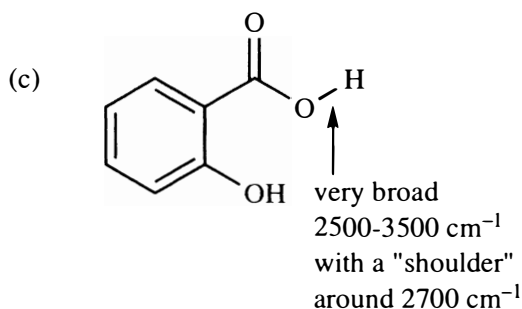
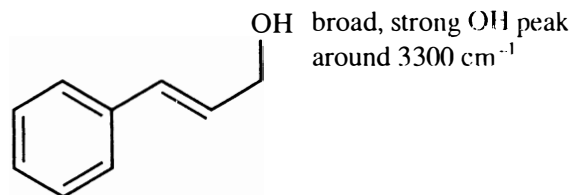
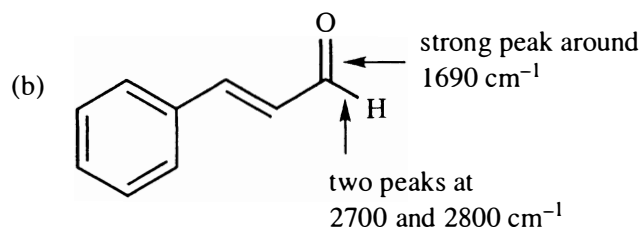
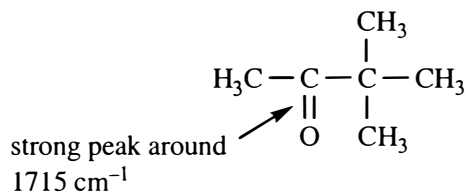
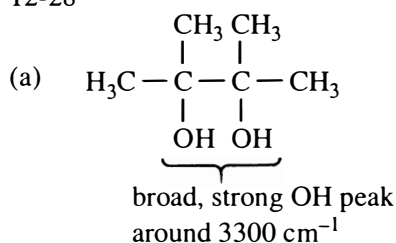
And there is! There is one piece—more specifically, one atom—that has mass 127: iodine! In all probability, the iodine atom is attached to a fragment of mass 71 which is C₅H₁₁, a pentyl group. We cannot tell with certainty what isomer it is, so unless there is some other evidence, let's propose a straight chain isomer, 1-iodopentane.



The 155 fragment probably has this bridged structure because iodine is so big:



12-28



If you wish to find IR spectra and mass spectra of common compounds, there are two web sites that are very helpful. Entering a name or molecular formula will give isomers from which to choose the desired structure and the IR or MS if available in their database.

<http://webbook.nist.gov/>

"NIST" is the U.S. National Institute of Standards and Technology.

<http://www.aist.go.jp/RIODB/SDBS/menu-e.html>

This is from the National Institute of Advanced Industrial Science and Technology of Japan.

CHAPTER 13—NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

A benzene ring can be written with three alternating double bonds or with a circle in the ring. All of the carbons and hydrogens in an unsubstituted benzene ring are equivalent, regardless of which symbolism is used.



equivalent to



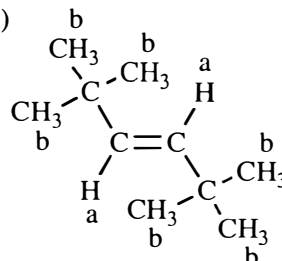
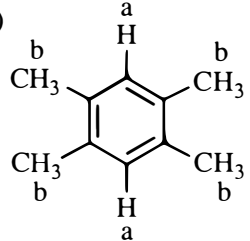
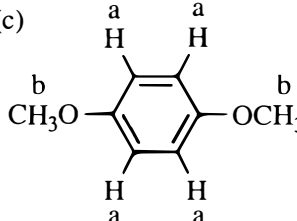
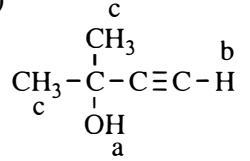
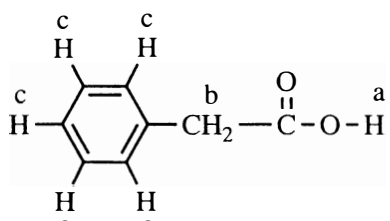
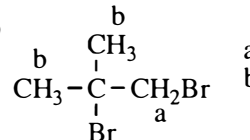
The Japanese web site listed at the bottom of p. 270 also gives proton and carbon NMR spectra.

Reminder: The word "spectrum" is singular; the word "spectra" is plural.

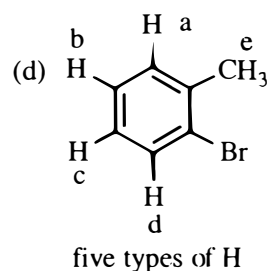
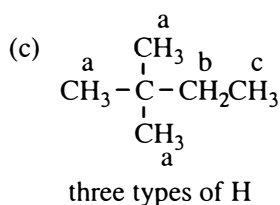
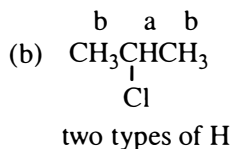
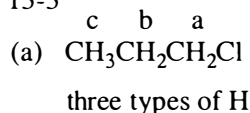
13-1

- (a) $\frac{650 \text{ Hz}}{300 \times 10^6 \text{ Hz}} = 2.17 \times 10^{-6} = 2.17 \text{ ppm downfield from TMS}$
- (b) Difference in magnetic field = $70,459 \text{ gauss} \times (2.17 \times 10^{-6}) = 0.153 \text{ gauss}$
- (c) The chemical shift does not change with field strength: $\delta 2.17$ at both 60 MHz and 300 MHz.
- (d) $(2.17 \text{ ppm}) \times (60 \text{ MHz}) = (2.17 \times 10^{-6}) \times (60 \times 10^6 \text{ Hz}) = 130 \text{ Hz}$

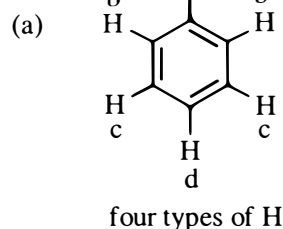
13-2 Numbers are chemical shift values, in ppm, derived from Table 13-3 and the Appendix in the text. Your predictions should be in the given range, or within 0.5 ppm of the given value.

- (a)  $a = \delta 5-6$
 $b = \delta 0.9$
- (b)  $a = \delta 7.2$
 $b = \delta 2.3$
- (c)  $a = \delta 7.2$
 $b = \delta 3.6$
- (d)  $a = \delta 2-5$
 $b = \delta 2.5$
 $c = \delta 1-2$
- (e)  $a = \delta 10-12$
 $b \approx \delta 3$ (between two deshielding groups)
 $c = \delta 7.2$ (The hydrogens labeled "c" are not equivalent. They appear at roughly the same chemical shift because the substituent is neither strongly electron-donating nor withdrawing.)
- (f)  $a = \delta 3-4$
 $b = \delta 1-2$

13-3



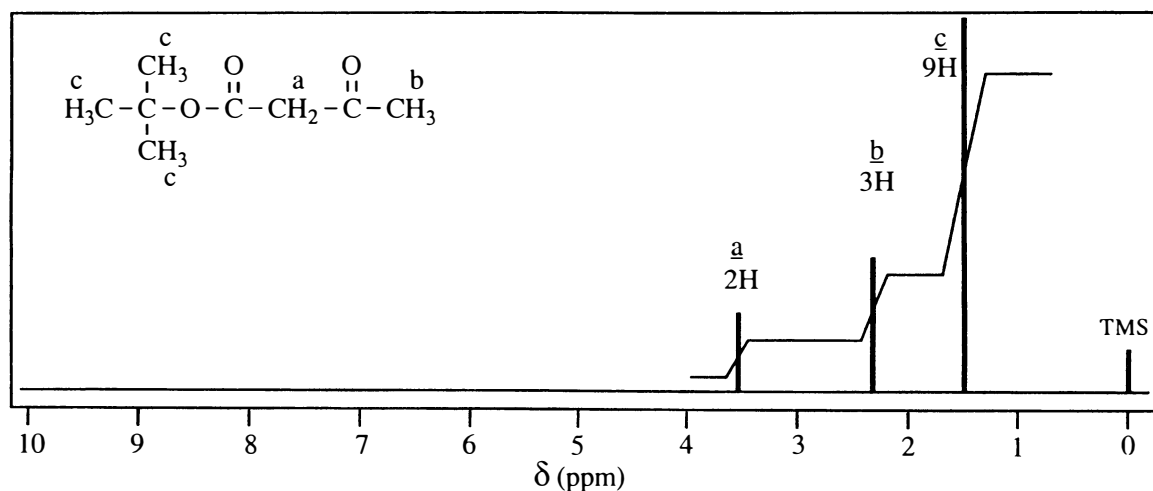
13-4



(b) The three types of aromatic hydrogens appear in a relatively small space around δ 7.2. The signal is complex because all the peaks from the three types of hydrogens overlap.

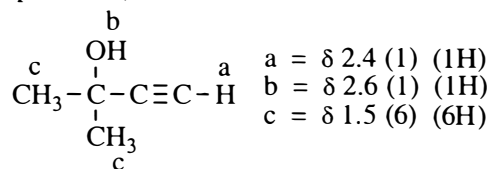
Note: NMR spectra drawn in this Solutions Manual will represent peaks as single lines. These lines may not look like "real" peaks, but this avoids the problem of variation among spectrometers and printers. Individual spectra may look different from the ones presented here, but all of the important information will be contained in these representational spectra.

13-5

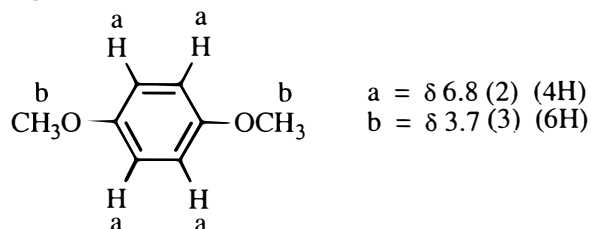


13-6 The three spectra are identified with their structures. Data are given as chemical shift values, with the integration ratios of each peak given in parentheses.

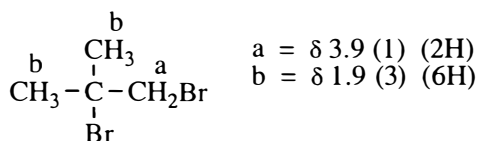
Spectrum (a)



Spectrum (b)

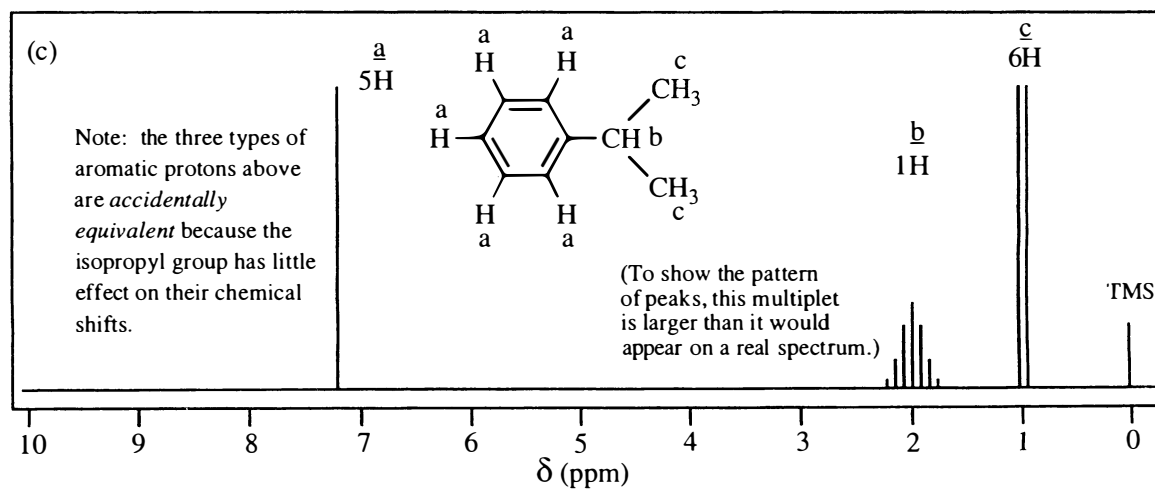
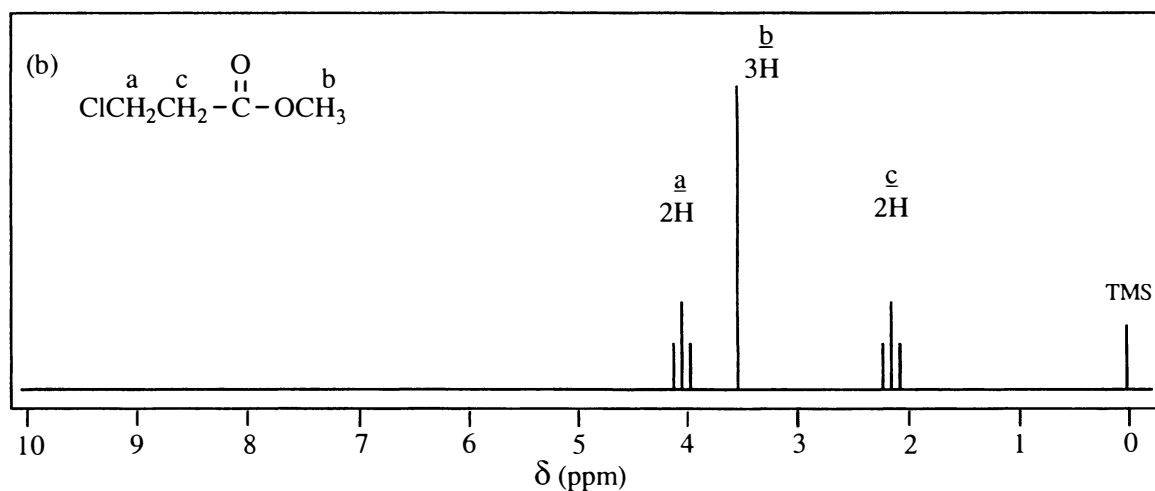
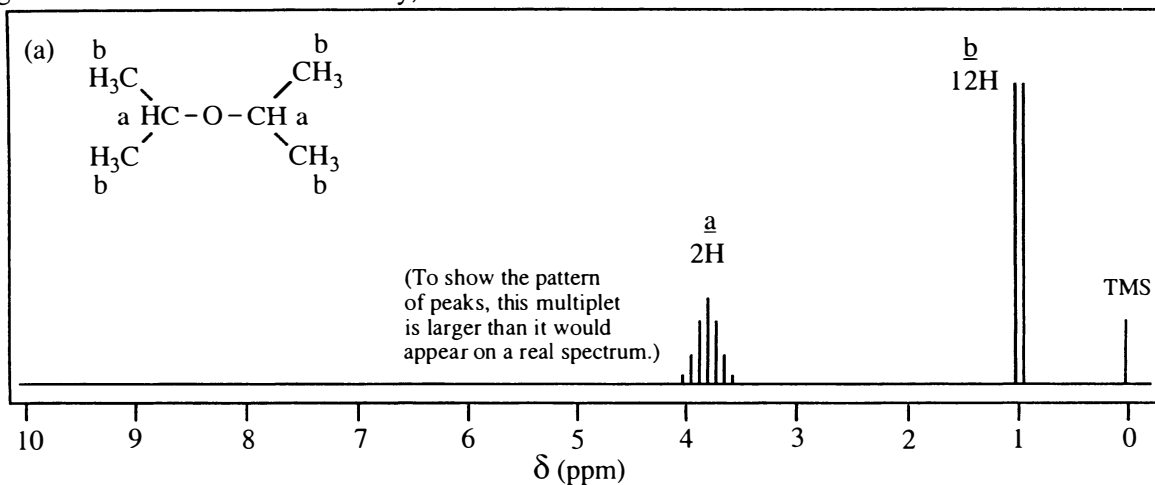


Spectrum (c)

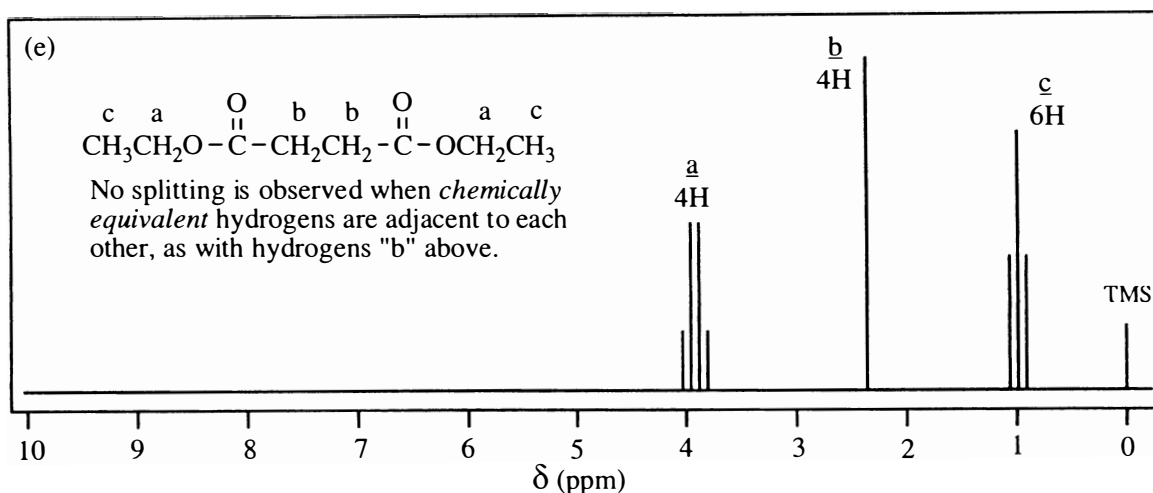
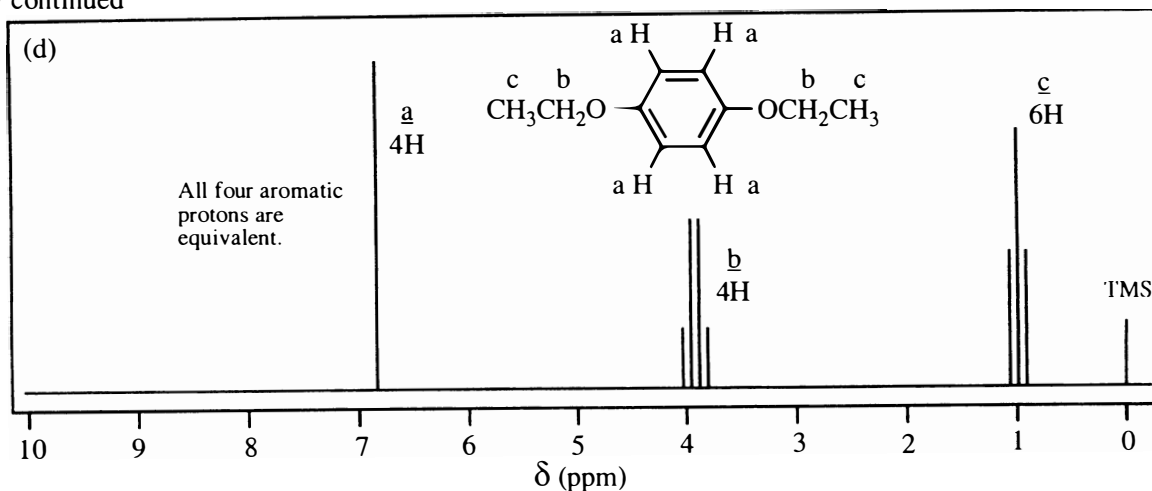


(This is the compound in Problem 13-2(f). You may wish to check your answer to that question against the spectrum.)

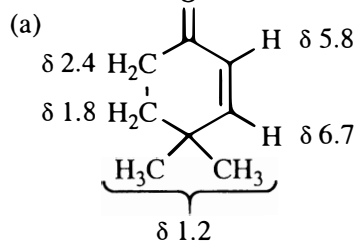
13-7 Chemical shift values are approximate and may vary slightly from yours. The splitting and integration values should match exactly, however.



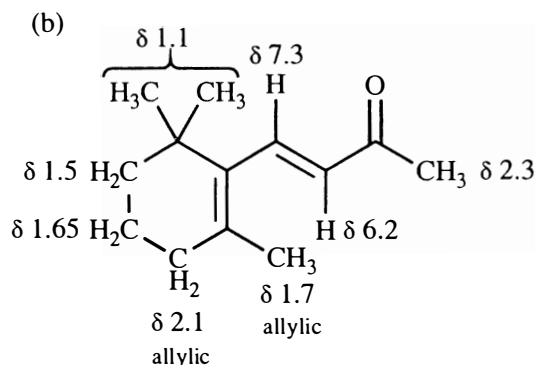
13-7 continued



13-8

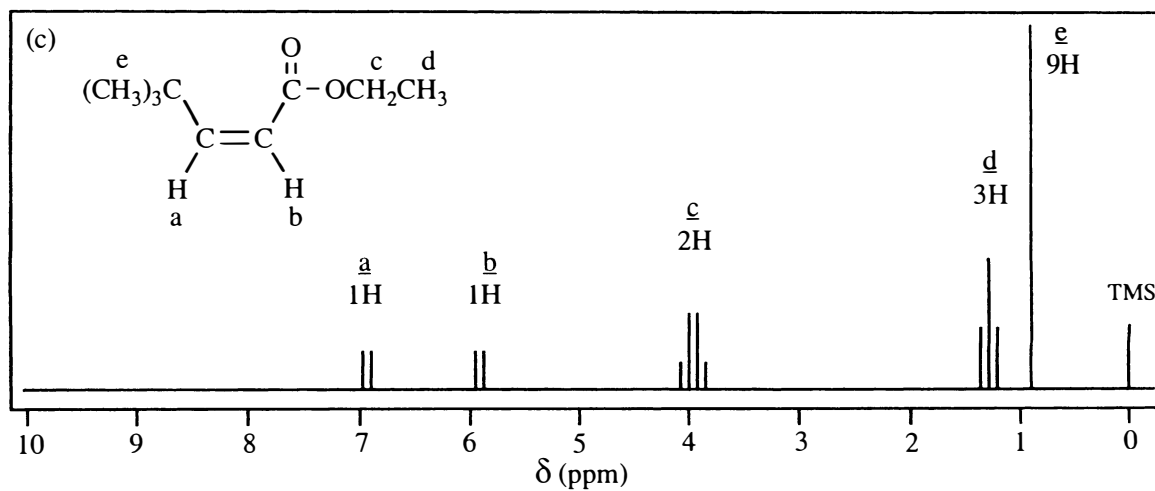
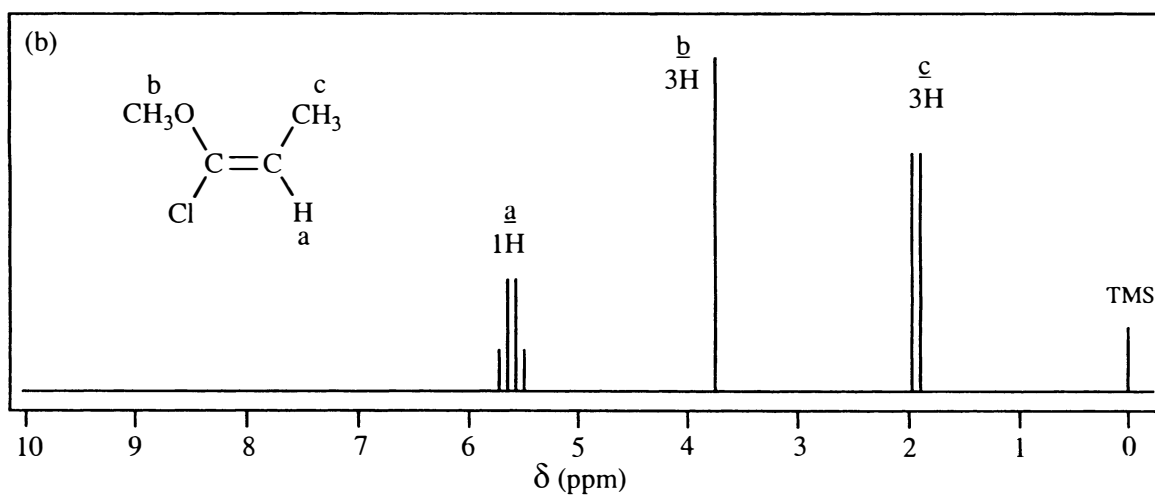
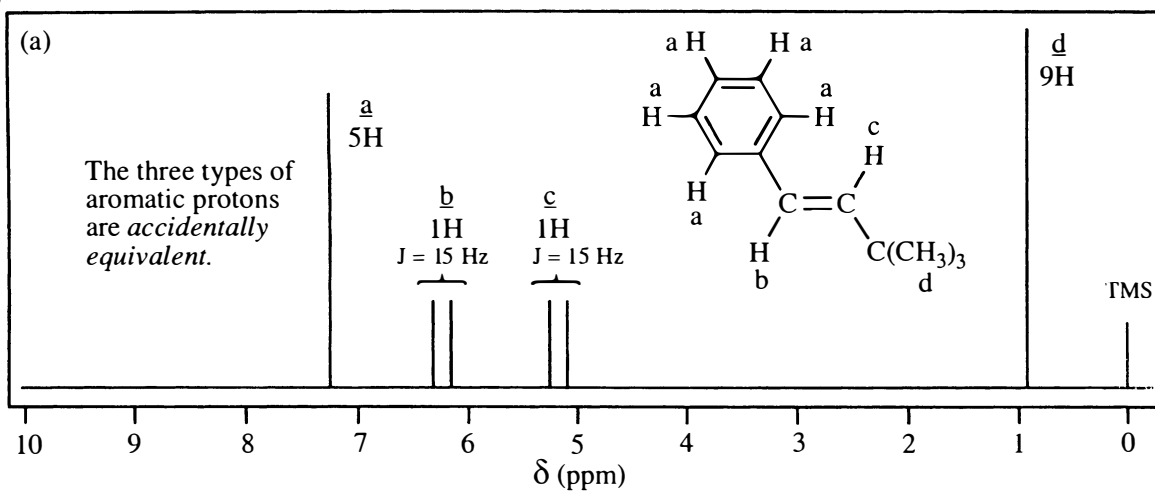


The signals at 1.8 and 2.4 are triplets because each set of protons has two neighboring hydrogens. The N+1 rule correctly predicts each to be a triplet.

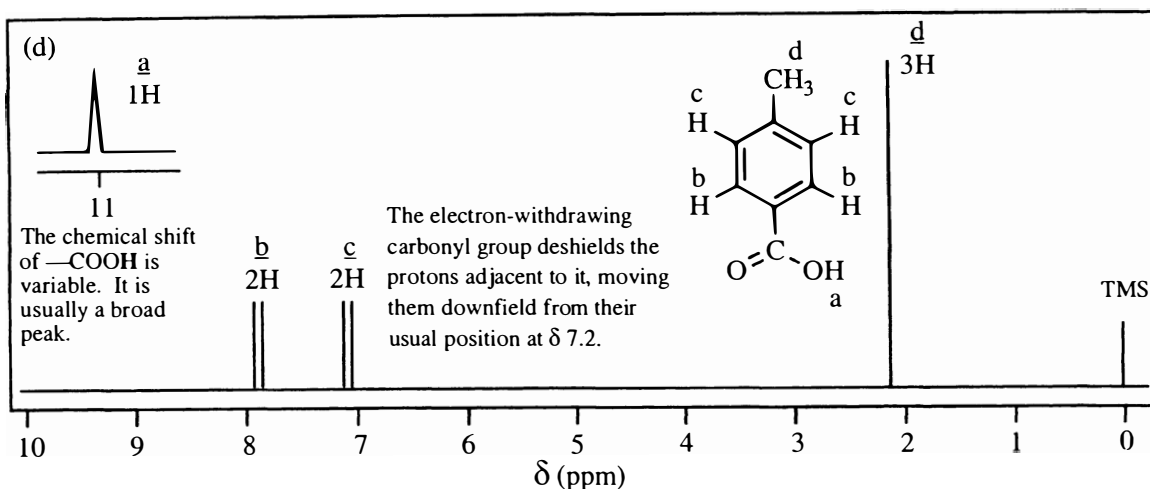


The three CH_2 groups can be distinguished by chemical shift and by splitting. The allylic CH_2 will be the farthest downfield of the three, at 2.1. The signal at 1.5 is a triplet, so that must be the one with only two neighboring protons. The CH_2 showing the multiplet at 1.65 must be the one between the other two CH_2 groups.

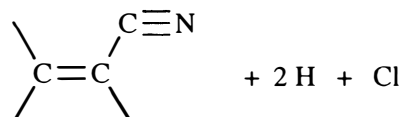
13-9



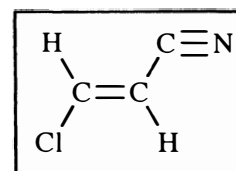
13-9 continued



13-10 The formula $\text{C}_3\text{H}_2\text{NCl}$ has three elements of unsaturation. The IR peak at 1650 cm^{-1} indicates an alkene, while the absorption at 2200 cm^{-1} must be from a nitrile (not enough carbons left for an alkyne). These two groups account for the three elements of unsaturation. So far, we have:

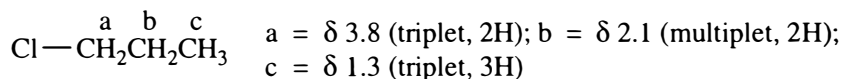


The NMR gives the coupling constant for the two protons as 14 Hz. This large J value shows the two protons as *trans* (*cis*, $J = 10\text{ Hz}$; geminal, $J = 2\text{ Hz}$). The structure must be the one in the box.

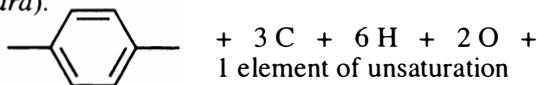


13-11

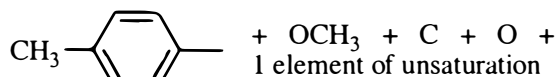
(a) $\text{C}_3\text{H}_7\text{Cl}$ —no elements of unsaturation; 3 types of protons in the ratio of 2 : 2 : 3 .



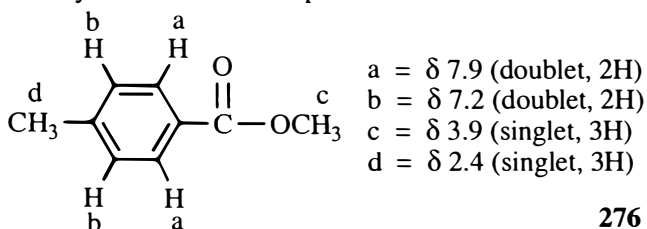
(b) $\text{C}_9\text{H}_{10}\text{O}_2$ —5 elements of unsaturation; four protons in the aromatic region of the NMR indicate a disubstituted benzene; the pair of doublets with $J = 8\text{ Hz}$ indicate the substituents are on opposite sides of the ring (*para*).



The other NMR signals are two 3H singlets, two CH_3 groups. One at $\delta 3.9$ must be a CH_3O group. The other at $\delta 2.4$ is most likely a CH_3 group on the benzene ring.

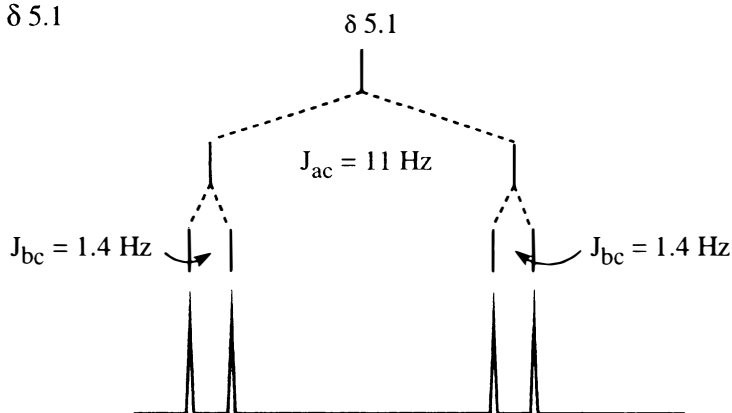


One way to assemble these pieces consistent with the NMR is:



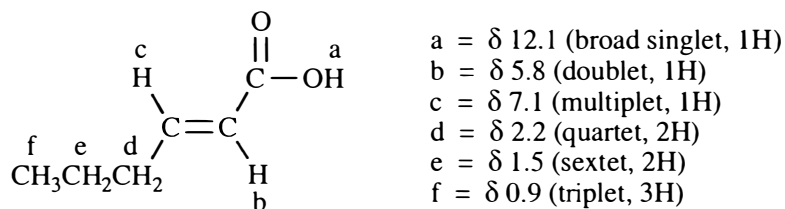
(Another plausible structure is to have the methoxy group directly on the ring and to put the carbonyl between the ring and the methyl. This does not fit the chemical shift values quite as well as the above structure, as the methyl would appear around $\delta 2.1$ or 2.2 instead of 2.4 .)

13-12 H_c , δ 5.1

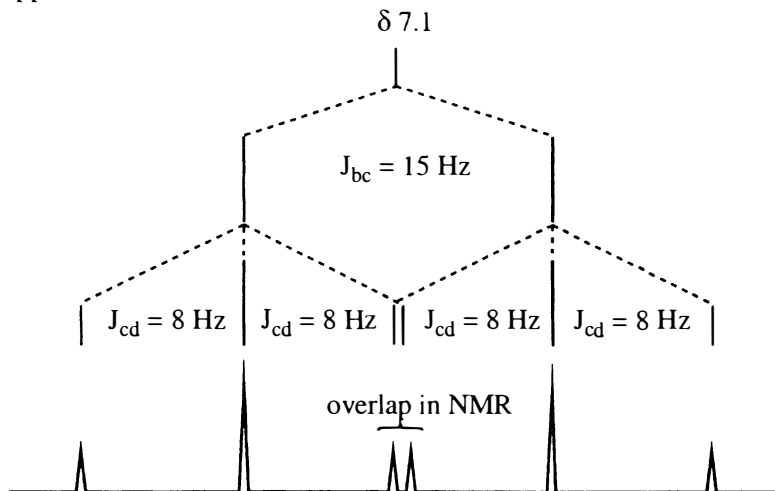


13-13

(a)

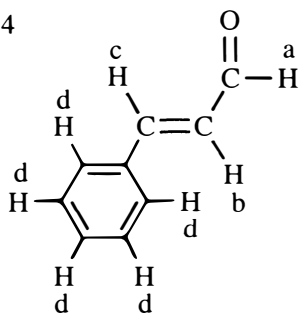


(b) The vinyl proton at δ 7.1 is H_c ; it is coupled with H_b and H_d , with two different coupling constants, J_{bc} and J_{cd} , respectively. The value of J_{bc} can be measured most precisely from the signal for H_b at δ 5.8; the two peaks are separated by about 15 Hz, corresponding to 0.05 ppm in a 300 MHz spectrum. The value of J_{cd} appears to be about the standard value 8 Hz, judging from the signal at δ 7.1. The splitting tree would thus appear:



13-14

(a)



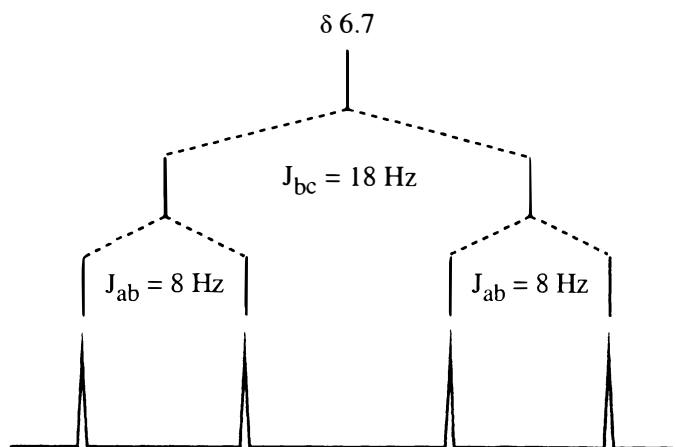
- $a = \delta 9.7$ (doublet, 1H)
 $b = \delta 6.7$ (doublet of doublets, 1H)
 $c = \delta 7.5$ (doublet, 1H)
 $d = \delta 7.4$ (multiple peaks, 5H)

The doublet for H_c at $\delta 7.4$ OVERLAPS the 5H peaks of H_d .

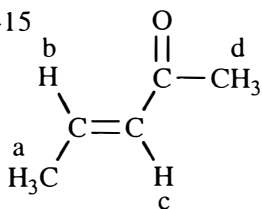
(b) J_{ab} can be determined most accurately from H_a at $\delta 9.7$: $J_{ab} \approx 8$ Hz, about the same as "normal" alkyl coupling.

J_{bc} can be measured from H_b at $\delta 6.7$, as the distance between either the first and third peaks or the second and fourth peaks (see diagram below): $J_{bc} \approx 18$ Hz, about double the "normal" alkyl coupling.

(c)



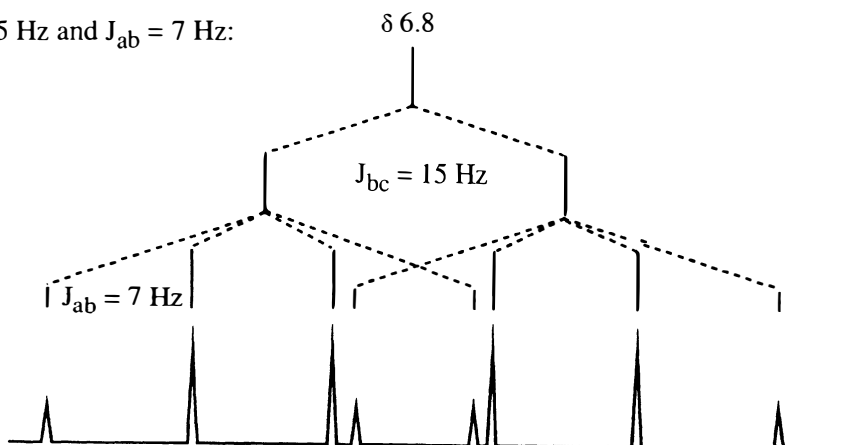
13-15



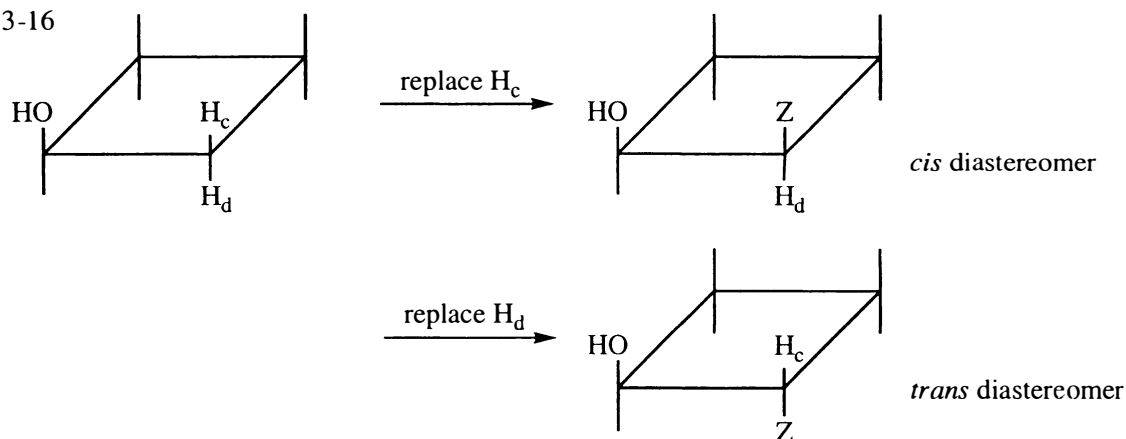
- (a) $a = \delta 1.7$
 $b \approx \delta 6.8$
 $c = \delta 5-6$
 $d = \delta 2.1$

- (b) $a =$ doublet
 $b =$ multiplet (two overlapping quartets—see part (c))
 $c =$ doublet
 $d =$ singlet

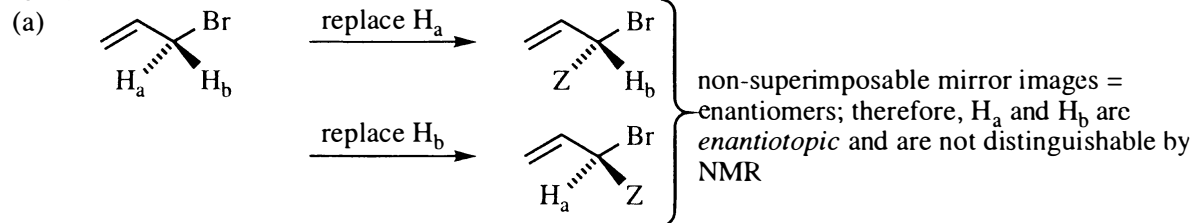
(c) using $J_{bc} = 15$ Hz and $J_{ab} = 7$ Hz:



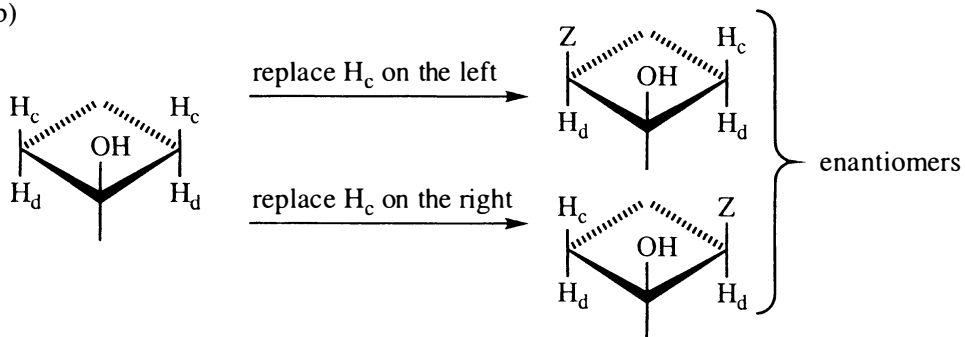
13-16



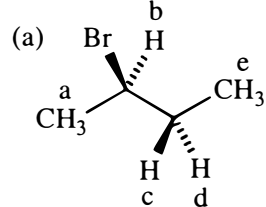
13-17



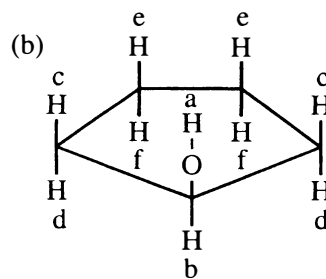
(b)

(c) The H_d protons are also enantiotopic.

13-18

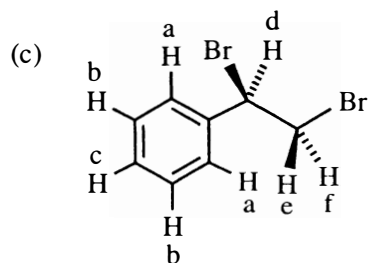


This compound has five types of protons. H_c and H_d are diastereotopic. $a = \delta 1.5$; $b = \delta 3.6$; $c, d = \delta 1.7$; $e = \delta 1.0$

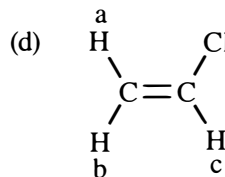


This compound has six types of protons. H_c and H_d are diastereotopic, as are H_e and H_f . $a = \delta 2.5$; $b = \delta 3.9$; $c, d = \delta 1.6$; $e, f = \delta 1.3$

13-18 continued

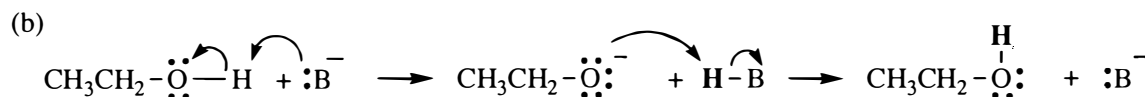
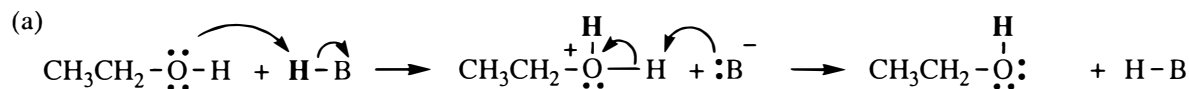


This compound has six types of protons.
 H_e and H_f are diastereotopic. $a, b, c = \delta 7.2$;
 $d \approx \delta 5.0$; $e, f = \delta 3.6$

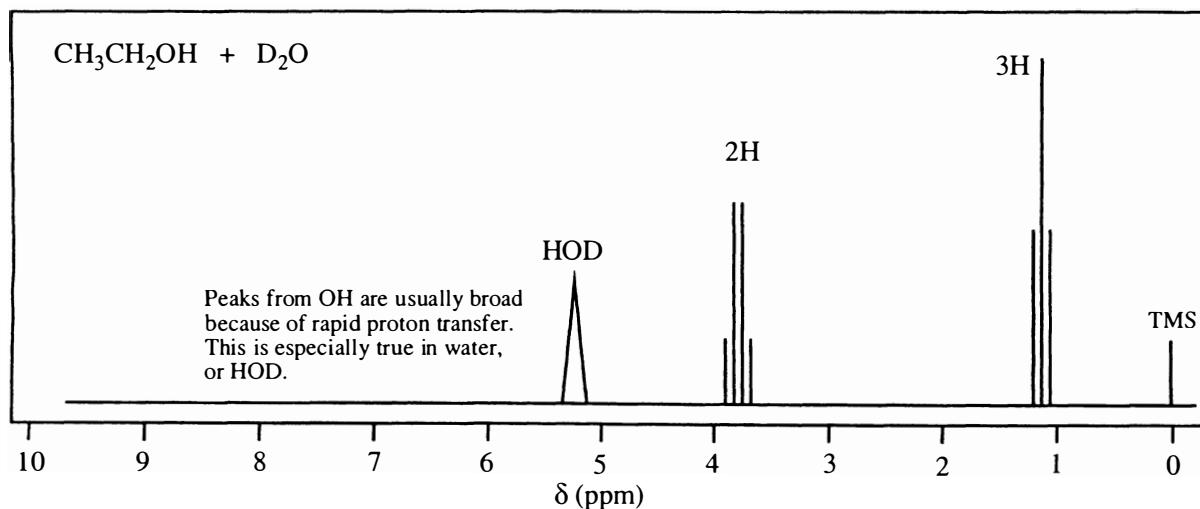
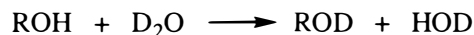


This compound has three types of protons. H_a and H_b are diastereotopic.
 $a, b = \delta 5-6$; $c = \delta 7-8$

13-19

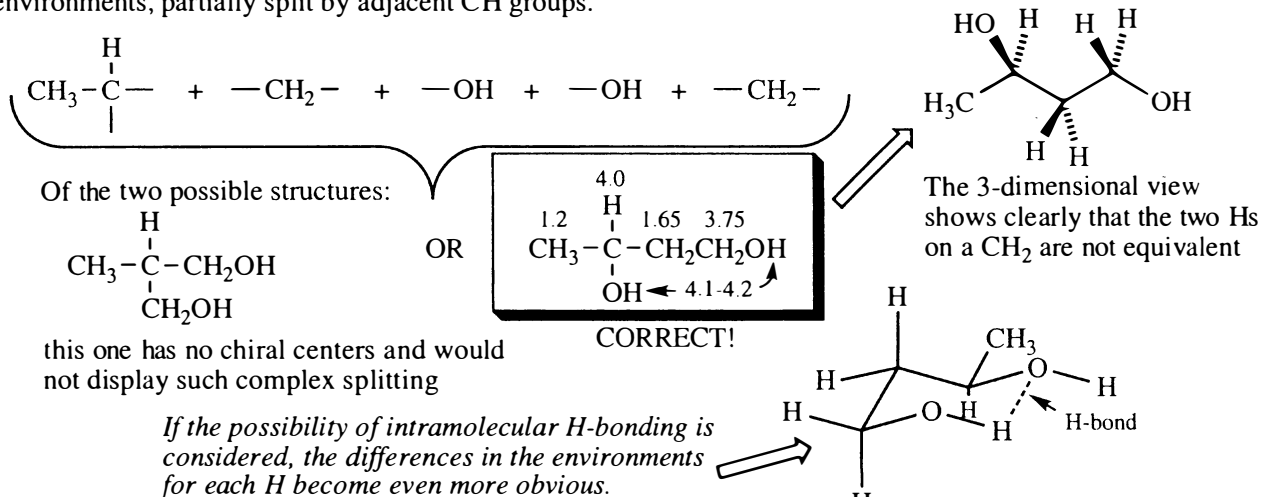


13-20 The protons from the OH in ethanol exchange with the deuteriums in D_2O . Thus, the OH in ethanol is replaced with OD which does not absorb in the NMR. What happens to the H? It becomes HOD which can usually be seen as a broad singlet around $\delta 5.25$. (If the solvent is CDCl_3 , the immiscible HOD will float on top of the solvent, out of the spectrometer beam, and its signal will be missing.)

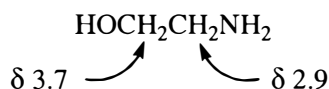


13-21

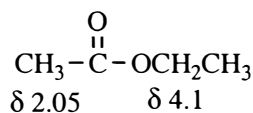
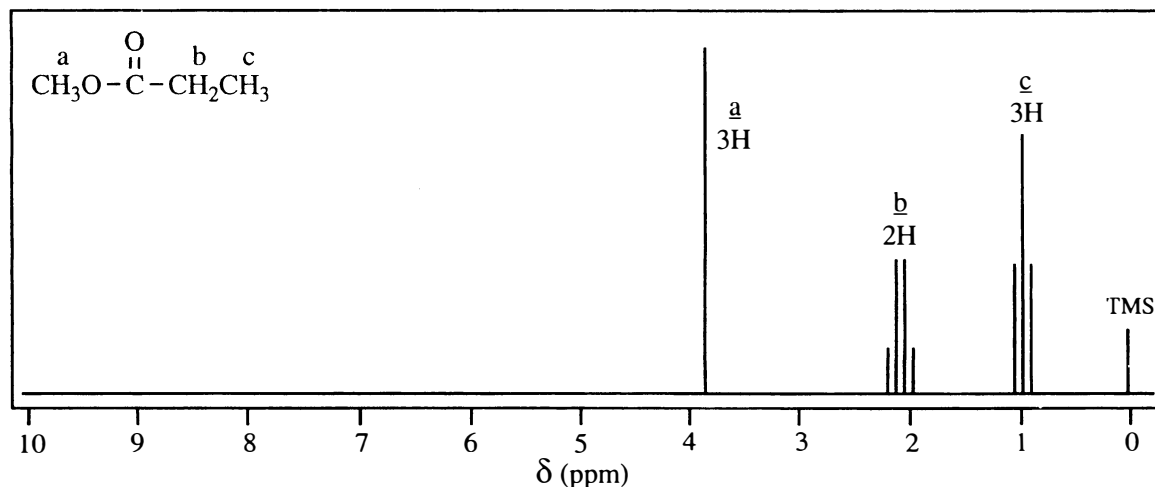
(a) The formula $C_4H_{10}O_2$ has no elements of unsaturation, so the oxygens must be alcohol or ether functional groups. The doublet at δ 1.2 represents 3H and must be a CH_3 next to a CH. The peaks centered at δ 1.65 integrating to 2H appear to be an uneven quartet and signify a CH_2 between two sets of non-equivalent protons; apparently the coupling constants between the non-equivalent protons are not equal, leading to a complicated pattern of overlapping peaks. The remaining five hydrogens appear in four groups of 1H, 1H, 1H, and 2H, between δ 3.7 and 4.2. The 2H multiplet at δ 3.75 is a CH_2 next to O, with complex splitting (doublet of doublets) due to diastereotopic neighbors. The 1H multiplet at δ 4.0 is a CH between many neighbors. The two 1H signals at δ 4.1-4.2 appear to be OH peaks in different environments, partially split by adjacent CH groups.



(b) The formula C_2H_7NO has no elements of unsaturation. The N must be an amine and the O must be an alcohol or ether. Two triplets, each with 2H, are certain to be $-CH_2CH_2-$. Since there are no carbons left, the N and O, with enough hydrogens to fill their valences, must go on the ends of this chain. The rapidly exchanging OH and NH_2 protons appear as a broad, 3H hump at δ 2.8.



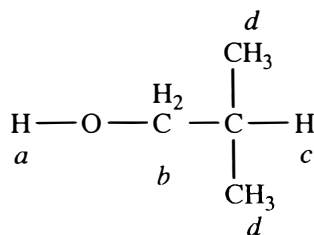
13-22



The key is what protons are adjacent to the oxygen. The CH_3O in methyl propanoate, above, absorbs at δ 3.9, whereas the CH_2 next to the carbonyl absorbs at δ 2.2. This is in contrast to ethyl acetate, at the left.

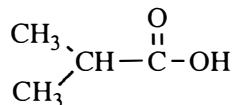
13-23

$H_a = \delta 2.4$ (singlet, 1H)
 $H_b = \delta 3.4$ (doublet, 2H)
 $H_c = \delta 1.8$ (multiplet, 1H)
 $H_d = \delta 0.9$ (doublet, 6H)

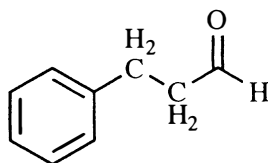


13-24

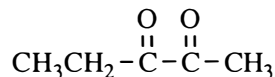
(a) The formula $\text{C}_4\text{H}_8\text{O}_2$ has one element of unsaturation. The 1H singlet at $\delta 12.1$ indicates carboxylic acid. The 1H multiplet and the 6H doublet scream isopropyl group.



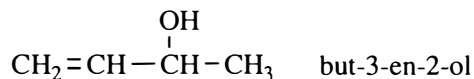
(b) The formula $\text{C}_9\text{H}_{10}\text{O}$ has five elements of unsaturation. The 5H pattern between $\delta 7.2$ -7.4 indicates monosubstituted benzene. The peak at $\delta 9.85$ is unmistakably an aldehyde, trying to be a triplet because it is weakly coupled to an adjacent CH_2 . The two triplets at $\delta 2.7$ -3.0 are adjacent CH_2 groups.



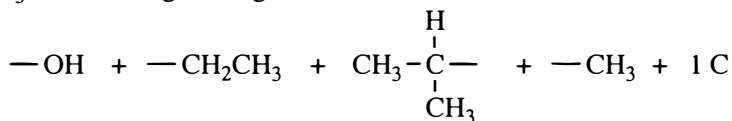
(c) The formula $\text{C}_5\text{H}_8\text{O}_2$ has two elements of unsaturation. A 3H singlet at $\delta 2.3$ is probably a CH_3 next to carbonyl. The 2H quartet and the 3H triplet are certain to be ethyl; with the CH_2 at $\delta 2.7$, this also appears to be next to carbonyl.



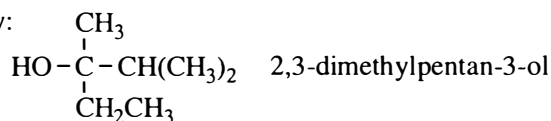
(d) The formula $\text{C}_4\text{H}_8\text{O}$ has one element of unsaturation, and the signals from $\delta 5.0$ -6.0 indicate a vinyl pattern ($\text{CH}_2=\text{CH}-$). The complex quartet for 1H at $\delta 4.3$ is a CH bonded to an alcohol, next to CH_3 . The OH appears as a 1H singlet at $\delta 2.5$, and the CH_3 next to CH is a doublet at $\delta 1.3$. Put together:



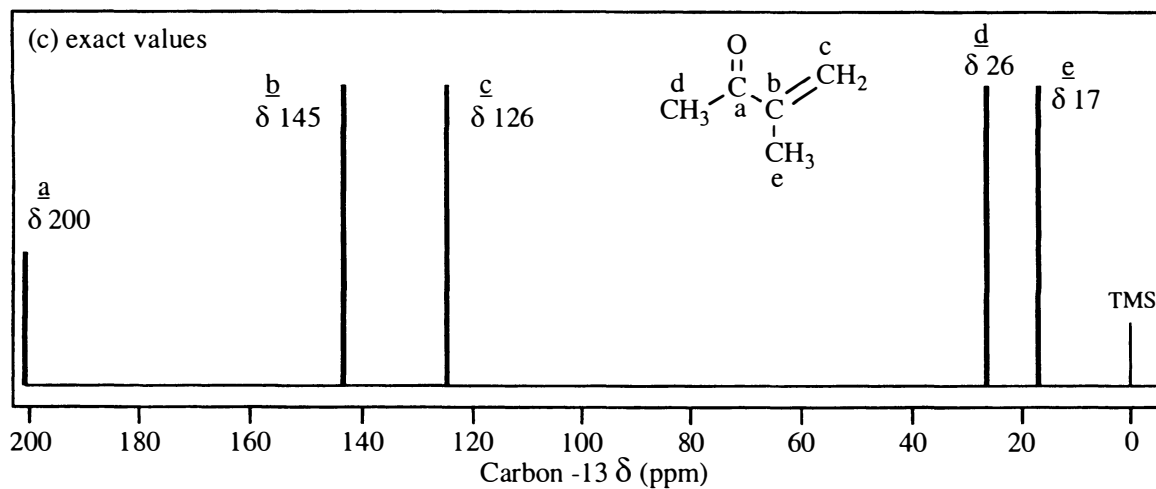
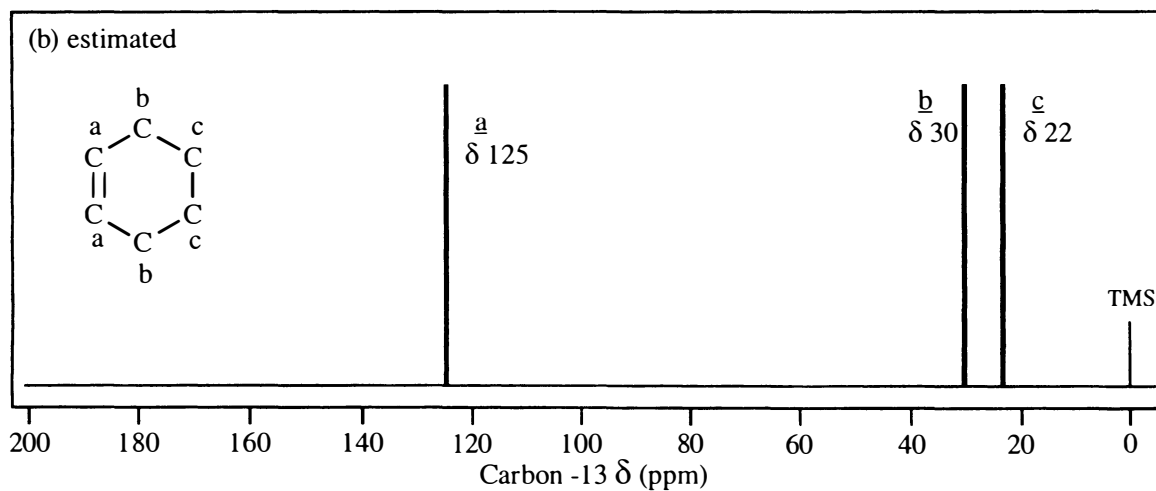
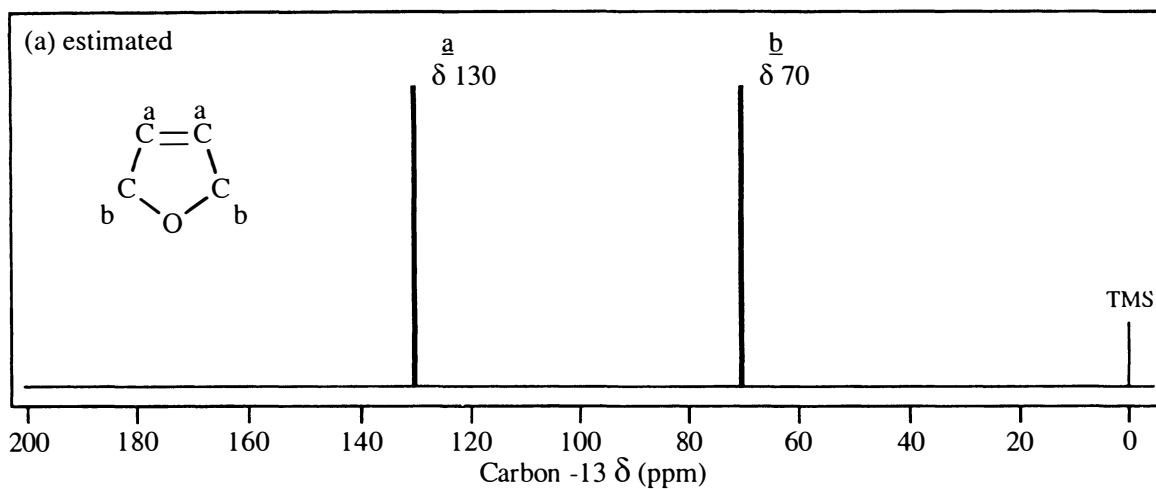
(e) The formula $\text{C}_7\text{H}_{16}\text{O}$ is saturated; the oxygen must be an alcohol or an ether, and the broad 1H peak at $\delta 1.2$ is probably an OH. Let's analyze the spectrum from left to right. The expansion of the 1H multiplet at $\delta 1.7$ shows seven peaks—an isopropyl group! Six of the nine H in the pattern at $\delta 0.9$ must be the doublet from the two methyls from the isopropyl. The 2H quartet at $\delta 1.5$ must be part of an ethyl pattern, from which the methyl triplet must be the other 3H of the pattern at $\delta 0.9$. This leaves only the 3H singlet at $\delta 1.1$ which must be a CH_3 with no neighboring Hs.



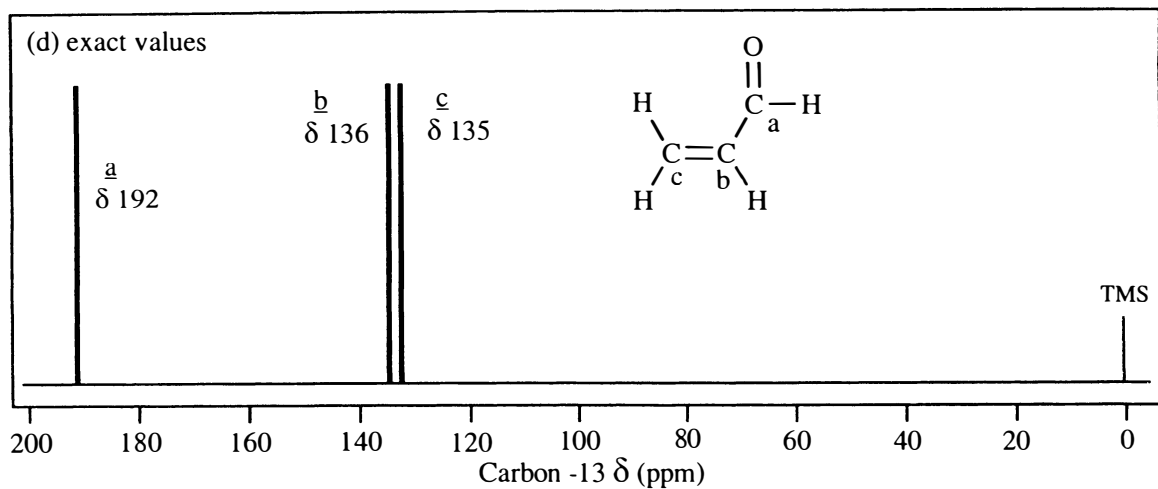
These pieces can be assembled in only one way:



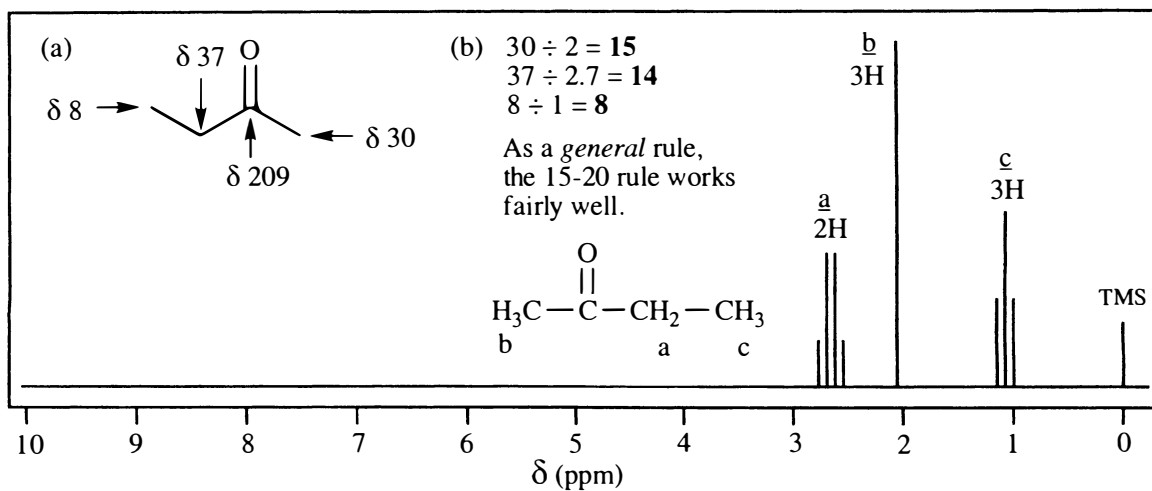
13-25 Chemical shift values are estimates from Figure 13-41 and from Appendix 1C, except in (c) and (d), where the values are exact.



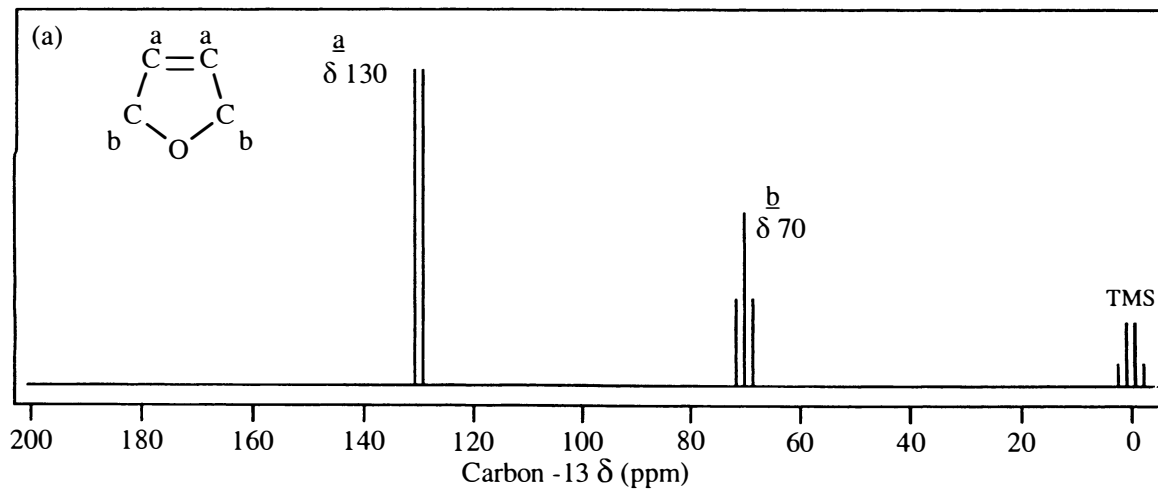
13-25 continued



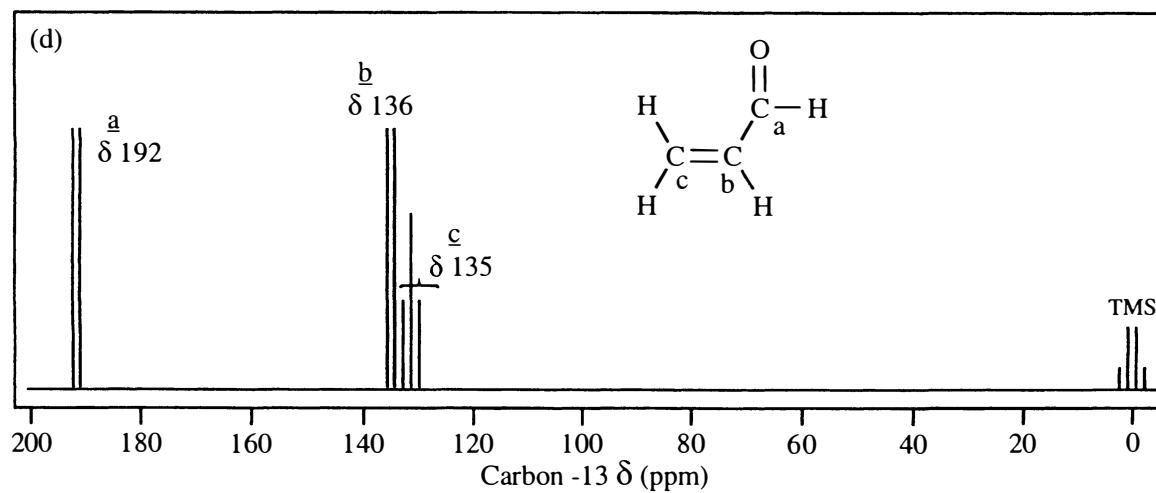
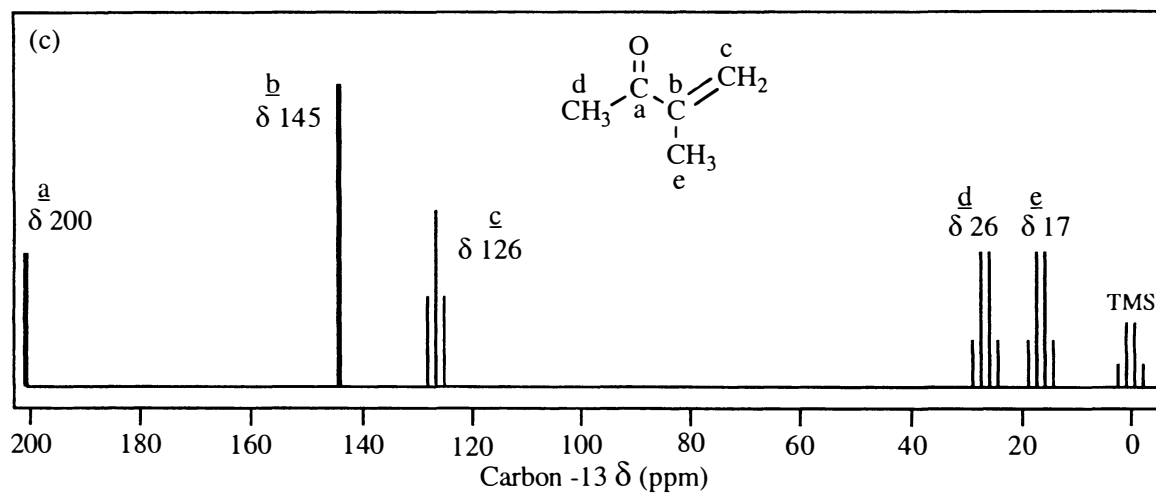
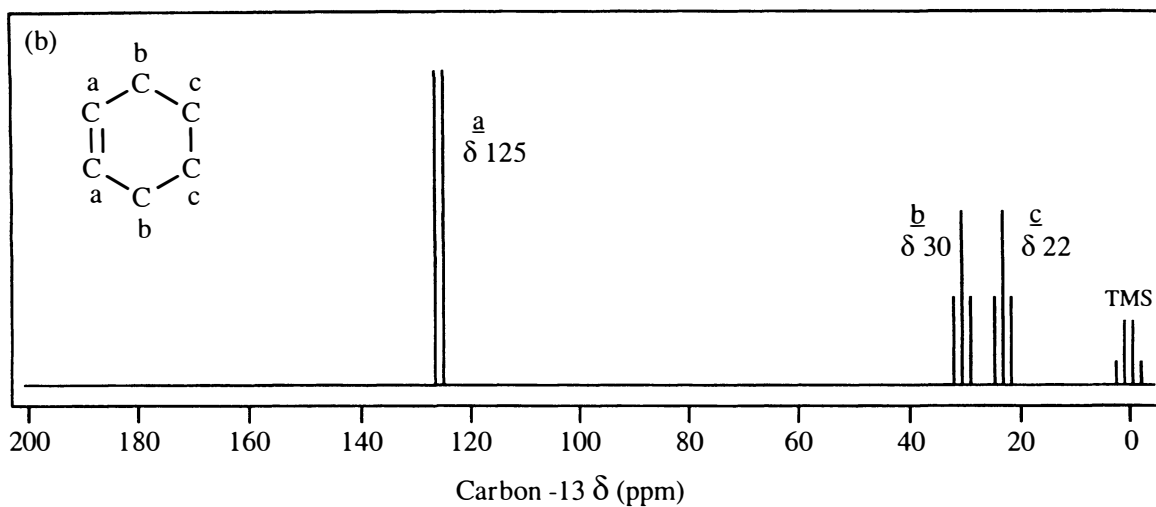
13-26



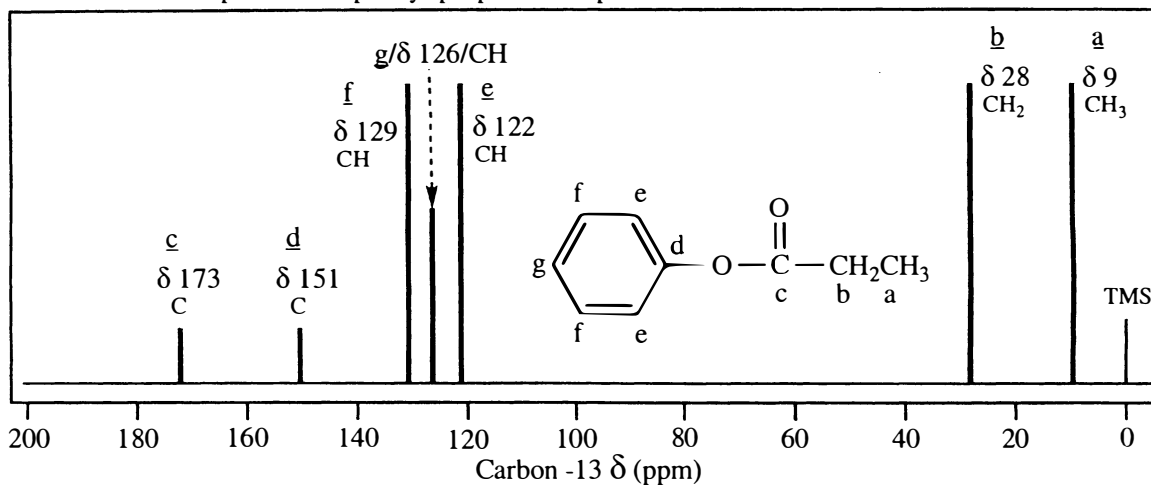
13-27



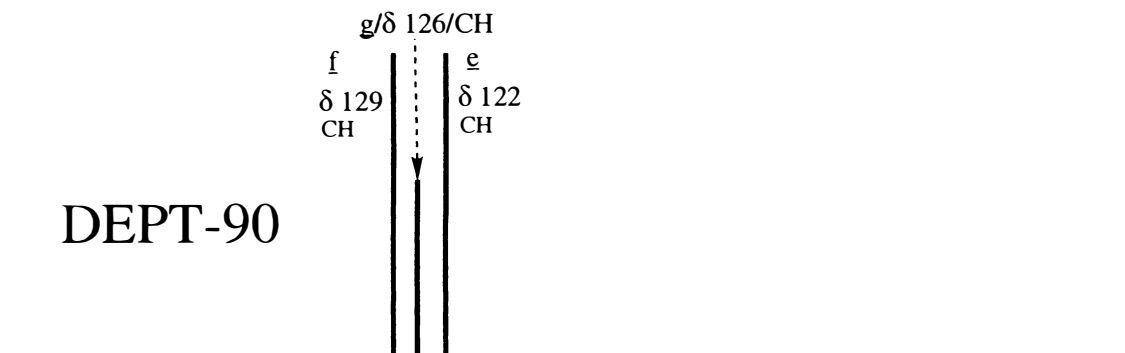
13-27 continued



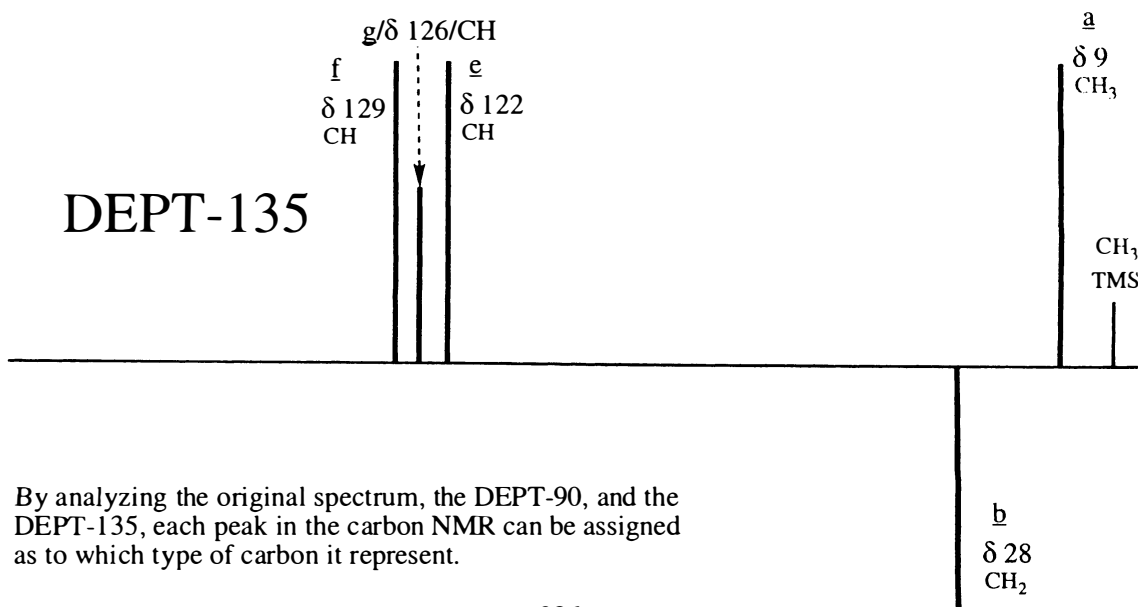
13-28 The full carbon spectrum of phenyl propanoate is presented below.



The DEPT-90 will show only the methine carbons, i.e., CH. All other peaks disappear.



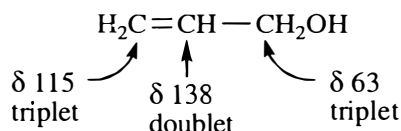
The DEPT-135 will show the methyl, CH_3 , and methine, CH, peaks pointed up, and the methylene, CH_2 , peaks pointed down.



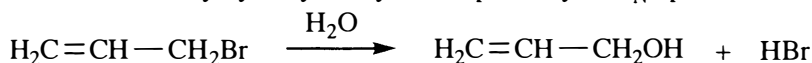
By analyzing the original spectrum, the DEPT-90, and the DEPT-135, each peak in the carbon NMR can be assigned as to which type of carbon it represents.

13-29

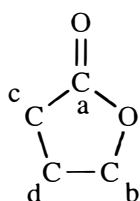
Since allyl bromide was the starting material, it is reasonable to expect the allyl group to be present in the impurity: the triplet at 115 is a $=CH_2$, the doublet at 138 is $=CH-$, and the triplet at 63 is a deshielded aliphatic CH_2 ; assembling the pieces forms an allyl group. The formula has changed from C_3H_5Br to C_3H_6O , so OH has replaced the Br.



Allyl bromide is easily hydrolyzed by water, probably an S_N1 process.



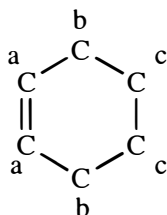
13-30



a = δ 180, singlet
b = δ 70, triplet
c = δ 28, triplet
d = δ 22, triplet

Two elements of unsaturation in $C_4H_6O_2$, one of which is a carbonyl, and no evidence of a $C=C$, prove that a ring must be present.

13-31



a = δ 128, doublet
b = δ 25, triplet
c = δ 23, triplet

Two elements of unsaturation in C_6H_{10} must be a $C=C$ and a ring. Only three peaks indicates symmetry.

Using PBr_3 instead of $H_2SO_4/NaBr$ would give a higher yield of bromocyclohexane.

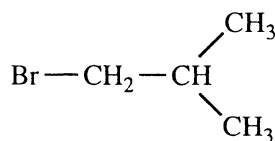
13-32 Compound 2

Mass spectrum: the molecular ion at m/z 136 shows a peak at 138 of about equal height, indicating a bromine atom is present: $136 - 79 = 57$. The fragment at m/z 57 is the base peak; this fragment is most likely a butyl group, C_4H_9 , so a likely molecular formula is C_4H_9Br .

Infrared spectrum: Notable for the absence of functional groups: no $O-H$, no $N-H$, no $=C-H$, no $C=C$, no $C=O \Rightarrow$ most likely an alkyl bromide.

NMR spectrum: The 6H doublet at δ 1.0 suggests two CH_3 's split by an adjacent H—an isopropyl group. The 2H doublet at δ 3.2 is a CH_2 between a CH and the Br.

Putting the pieces together gives isobutyl bromide.



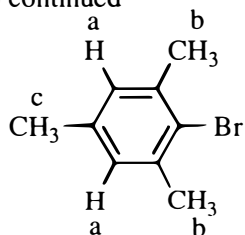
13-33

The formula $C_9H_{11}Br$ indicates four elements of unsaturation, just enough for a benzene ring.

Here is the most accurate method for determining the number of protons per signal from integration values *when the total number of protons is known*. Add the integration heights: $4.4 \text{ cm} + 13.0 \text{ cm} + 6.7 \text{ cm} = 24.1 \text{ cm}$. Divide by the total number of hydrogens: $24.1 \text{ cm} \div 11H = 2.2 \text{ cm/H}$. Each 2.2 cm of integration height = 1H, so the ratio of hydrogens is 2 : 6 : 3.

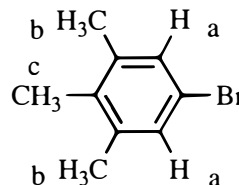
The 2H singlet at δ 7.1 means that only two hydrogens remain on the benzene ring, that is, it has 4 substituents. The 6H singlet at δ 2.3 must be two CH_3 's on the benzene ring in identical environments. The 3H singlet at δ 2.2 is another CH_3 in a slightly different environment from the first two. Substitution of the three CH_3 's and the Br in the most symmetric way leads to the structures on the next page.

13-33 continued

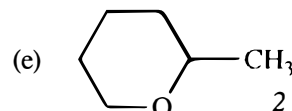
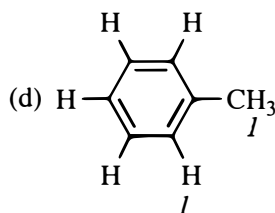
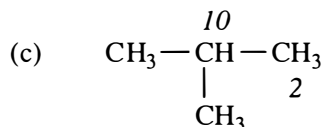
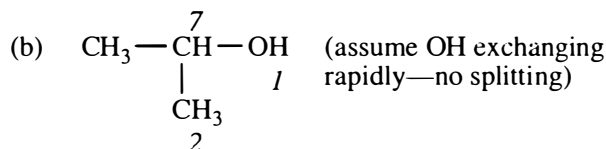
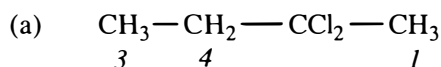


a = δ 7.1 (singlet, 2H)
 b = δ 2.3 (singlet, 6H)
 c = δ 2.2 (singlet, 3H)

a second structure is also possible although it is less likely because the Br would probably deshield the Hs labeled "a" to about 7.3-7.4

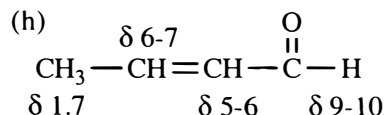
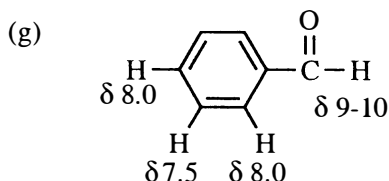
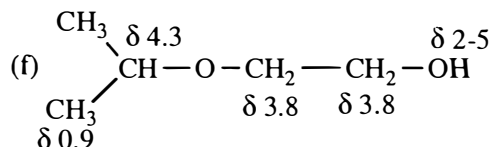
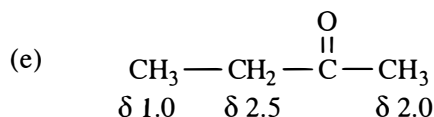
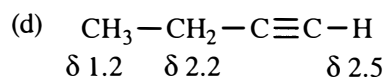
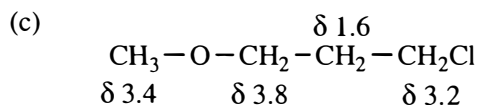
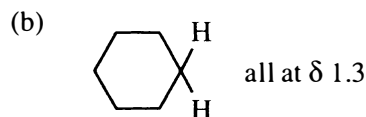
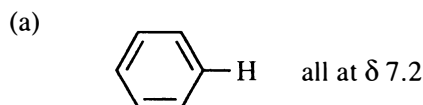


13-34 The numbers in italics indicate the number of peaks in each signal.



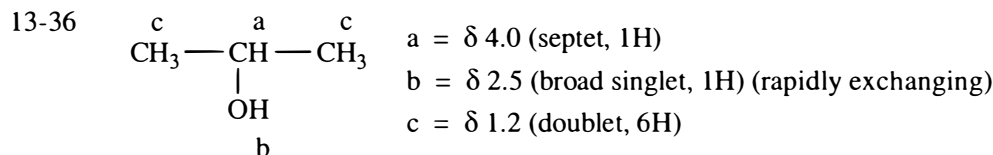
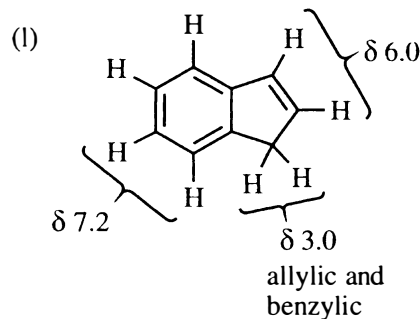
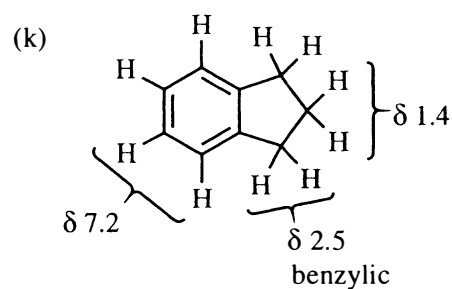
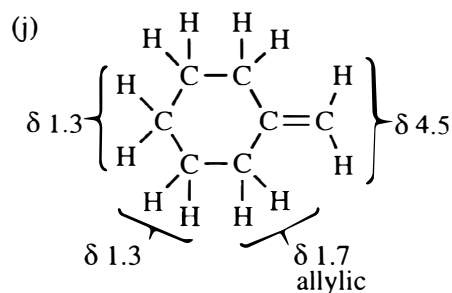
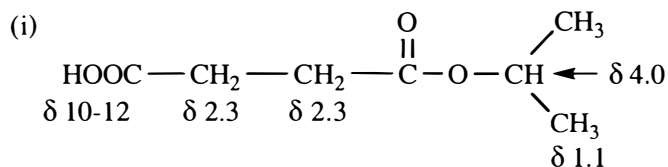
(all of these benzene H's are accidentally equivalent and do not split each other)

13-35 Consult Appendix 1 in the text for chemical shift values. *Your predictions should be in the given range, or within 0.5 ppm of the given value.*



The C=O has its strongest deshielding effect at the adjacent H (ortho) and across the ring (para). The remaining H (meta) is less deshielded.

13-35 continued

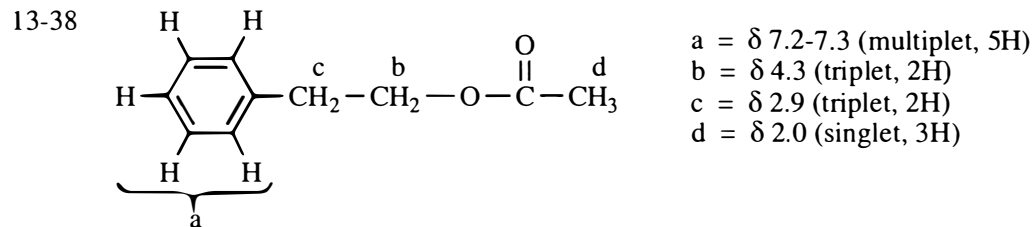


13-37

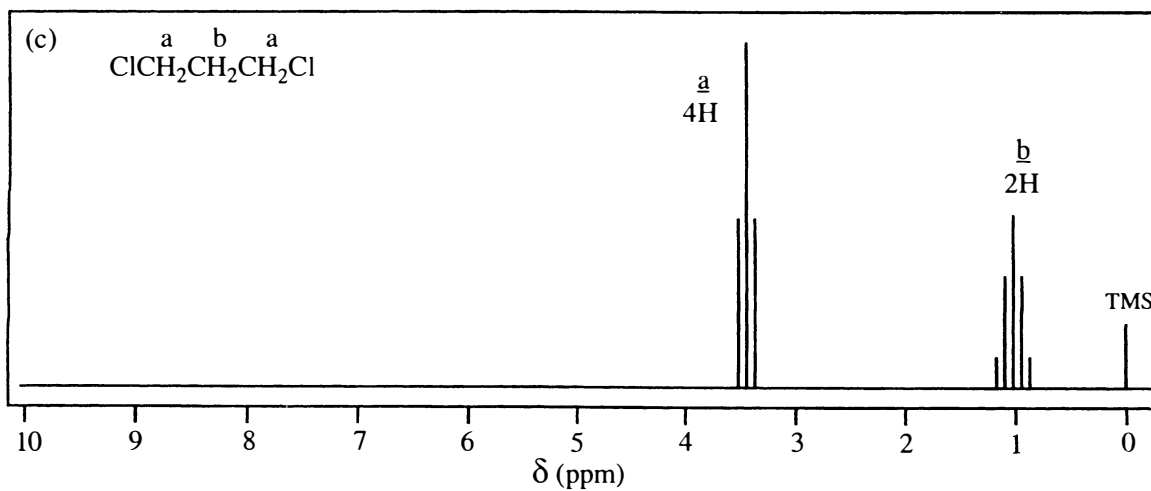
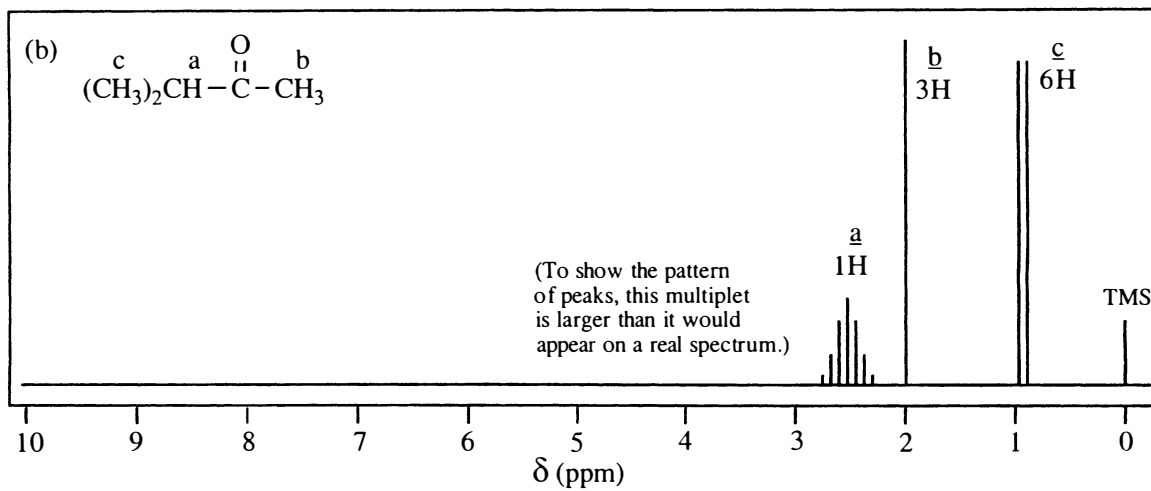
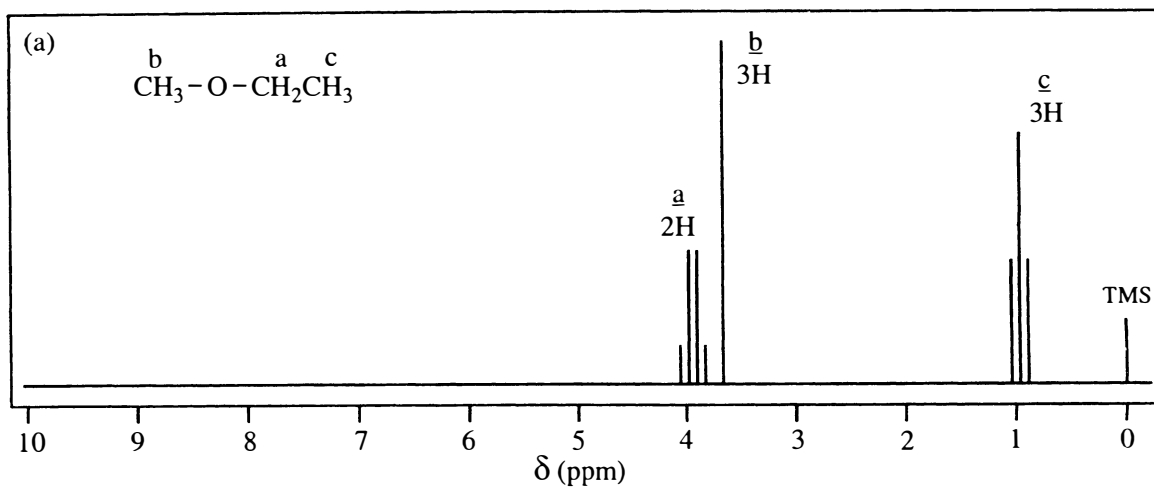
- (a) The chemical shift *in ppm* would not change: $\delta 4.00$.
- (b) Coupling constants do not change with field strength: $J = 7$ Hz, regardless of field strength.
- (c) At 60 MHz, $\delta 4.00 = 4.00 \text{ ppm} = (4.00 \times 10^{-6}) \times (60 \times 10^6 \text{ Hz}) = 240 \text{ Hz}$
 The signal is 240 Hz downfield from TMS in a 60 MHz spectrum.

At 300 MHz, $(4.00 \times 10^{-6}) \times (300 \times 10^6 \text{ Hz}) = 1200 \text{ Hz}$

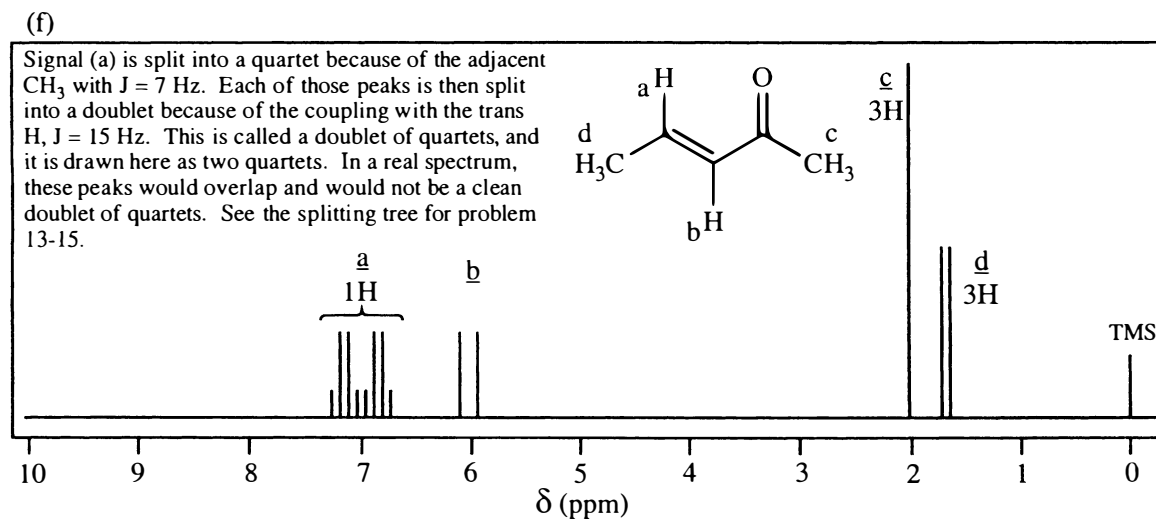
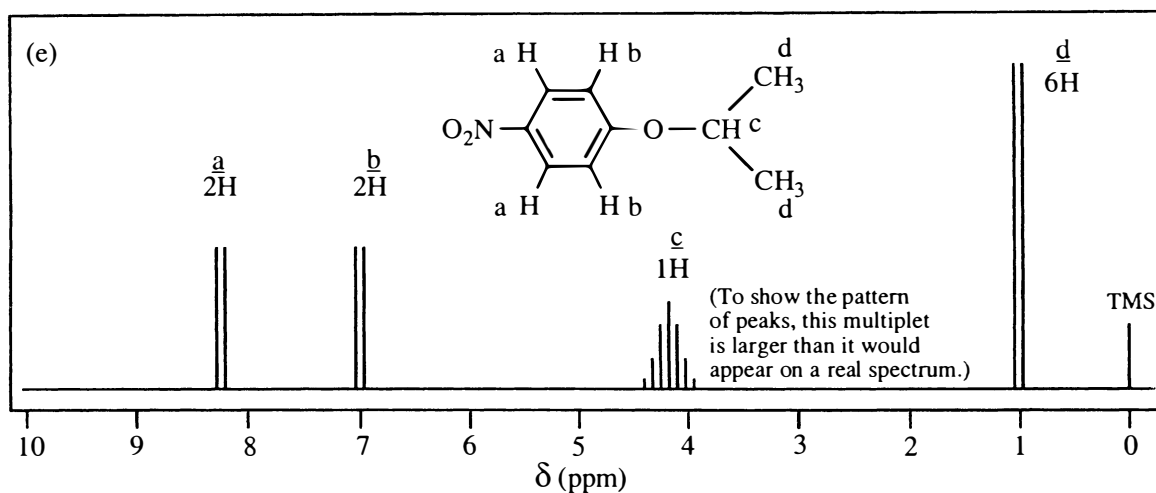
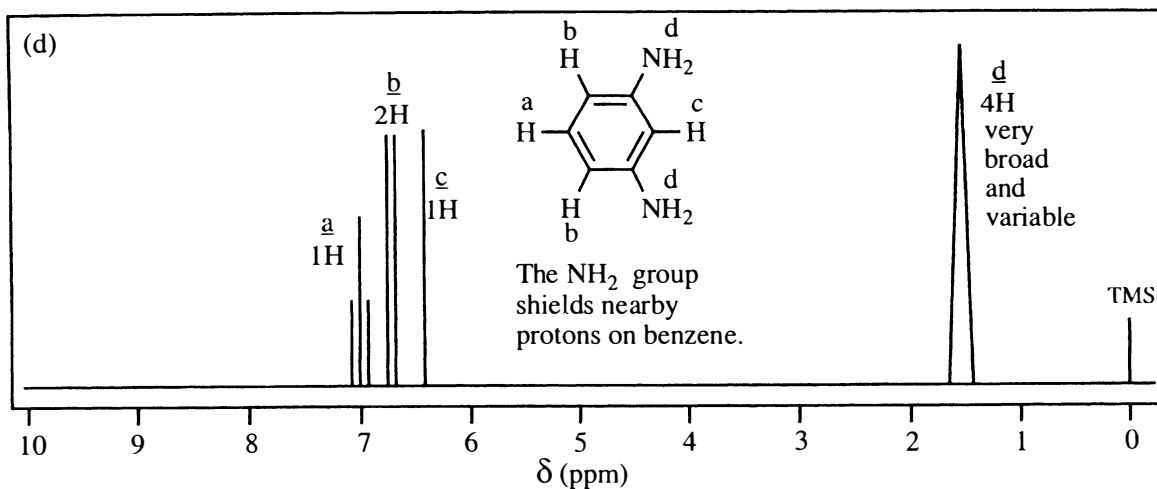
The signal is 1200 Hz downfield from TMS in a 300 MHz spectrum.
 Necessarily, 1200 Hz is exactly 5 times 240 Hz because 300 MHz is exactly 5 times 60 MHz. They are directly proportional.



13-39



13-39 continued



13-40

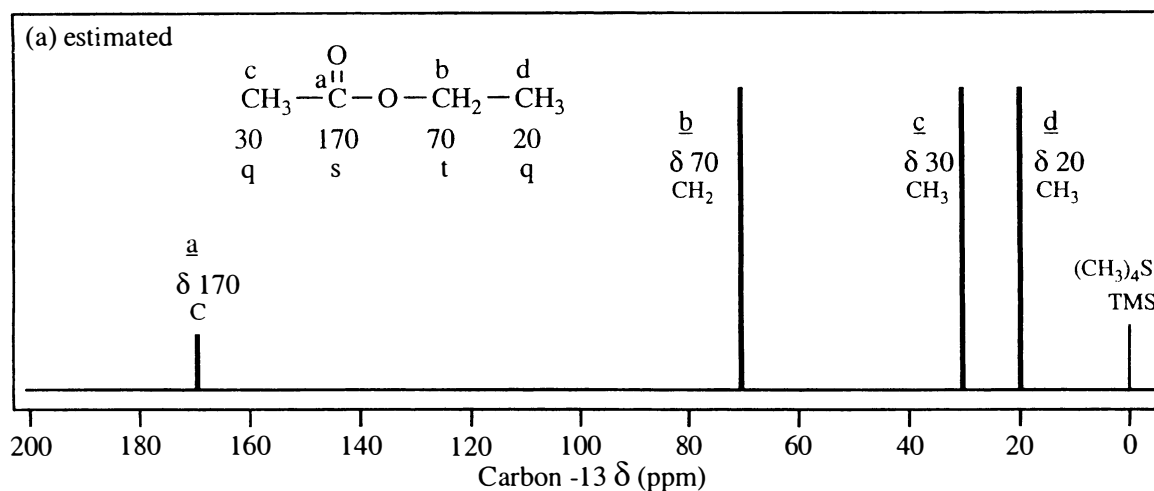
(a) The NMR of 1-bromopropane would have three sets of signals, whereas the NMR of 2-bromopropane would have only two sets (a septet and a doublet, the typical isopropyl pattern).

(b) Each spectrum would have a methyl singlet at δ 2. The left structure would show an ethyl pattern (a 2H quartet and a 3H triplet), whereas the right structure would exhibit an isopropyl pattern (a 1H septet and a 6H doublet).

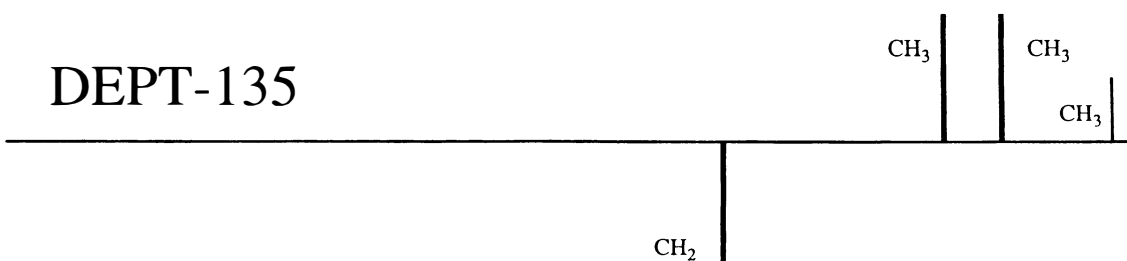
(c) The most obvious difference is the chemical shift of the CH_3 singlet. In the compound on the left, the CH_3 singlet would appear at δ 2.1, while the compound on the right would show the CH_3 singlet at δ 3.8. Refer to the solution of 13-22 for the spectrum of the second compound.

(d) The splitting and integration for the peaks in these two compounds would be identical, so the chemical shift must make the difference. As described in text section 13-5B, the alkyne is not nearly as deshielding as a carbonyl, so the protons in pent-2-yne would be farther upfield than the protons in butan-2-one, by about 0.5 ppm. For example, the methyl on the carbonyl would appear near δ 2.1 while the methyl on the alkyne would appear about δ 1.7.

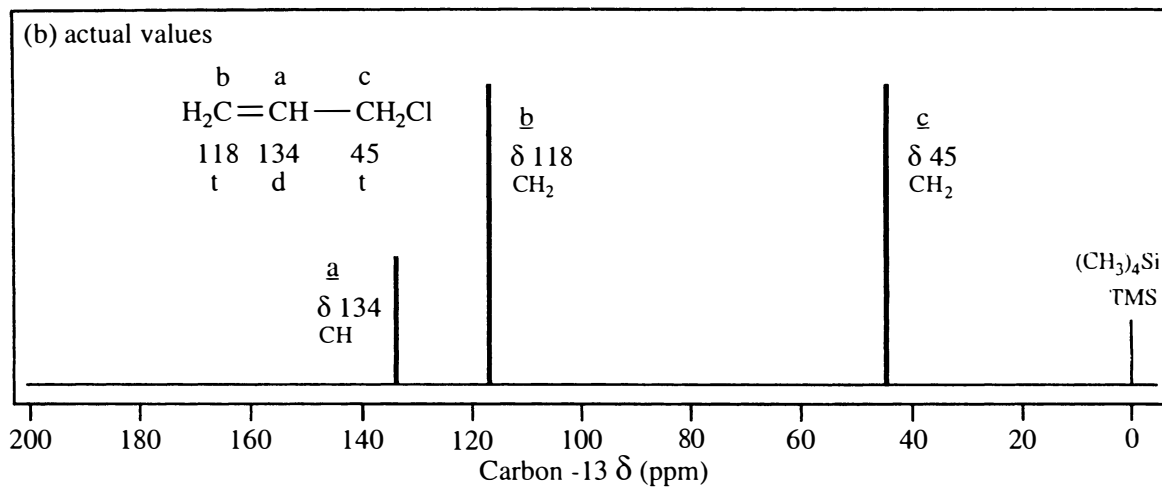
13-41 The multiplicity in the off-resonance decoupled spectrum is given below each chemical shift: s = singlet; d = doublet; t = triplet; q = quartet. It is often difficult to predict exact chemical shift values; your predictions should be in the right vicinity. There should be no question about the multiplicity and DEPT spectra, however.



The DEPT-90 spectrum for ethyl acetate would have no peaks because there are no CH groups.



13-41 continued



DEPT-90

CH

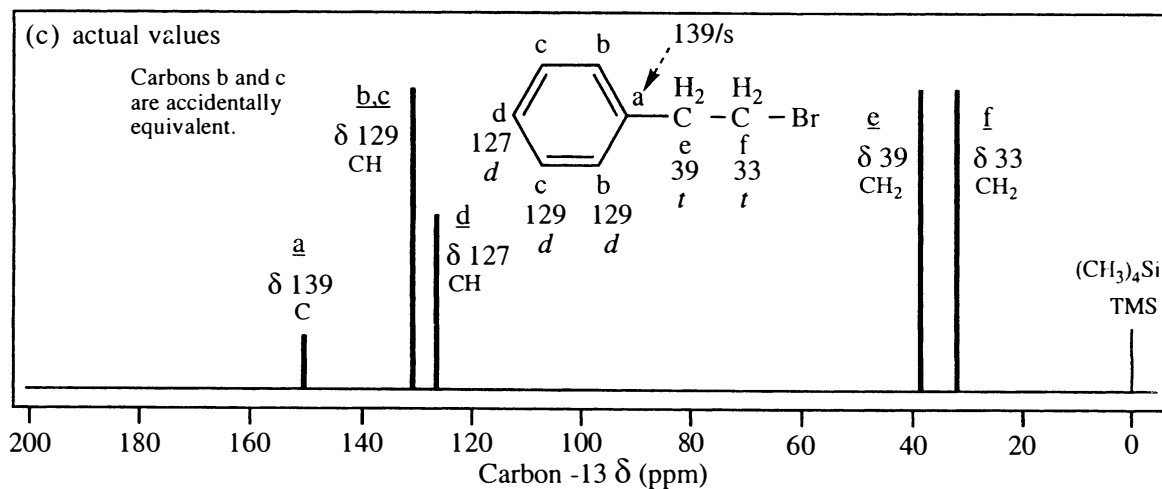
DEPT-135

CH

CH₃

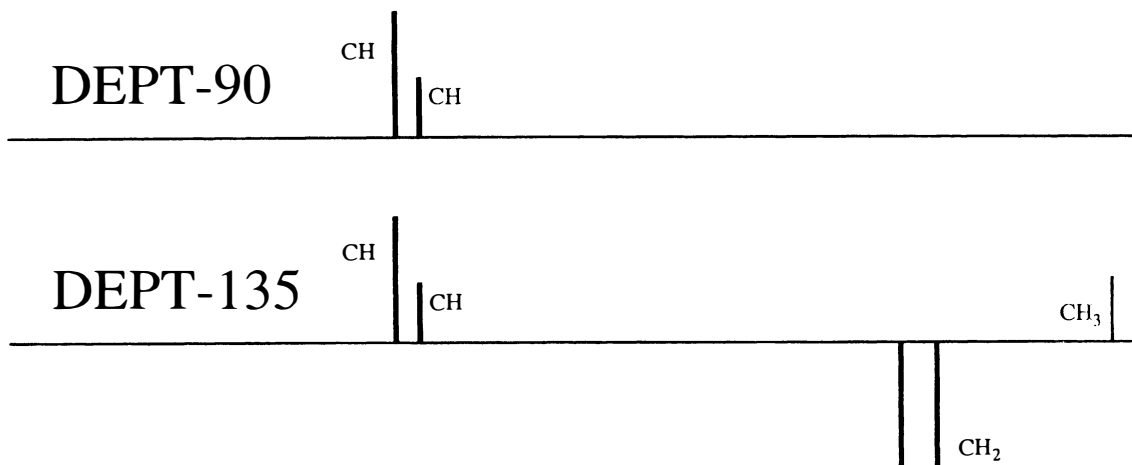
CH₂

CH₂

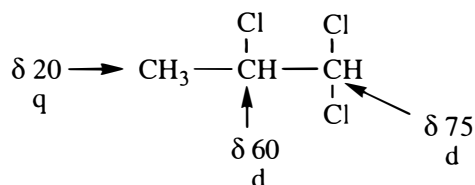


DEPT-90 and DEPT-135 on next page

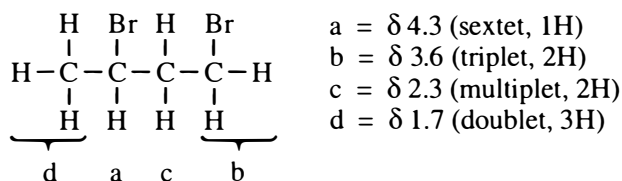
13-41 (c) continued



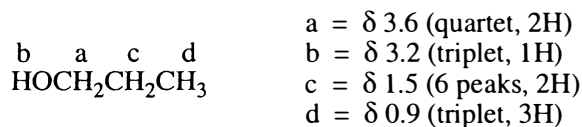
13-42 The multiplicity of the peaks in this off-resonance decoupled spectrum show two different CH's and a CH₃. There is only one way to assemble these pieces with three chlorines.



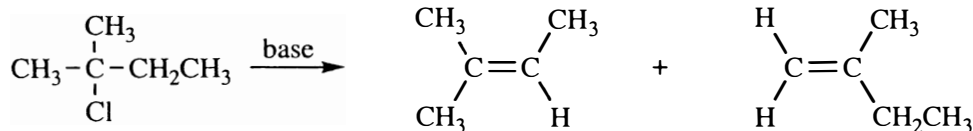
13-43 There is no evidence for vinyl hydrogens, so the double bond is gone. Integration gives eight hydrogens, so the formula must be C₄H₈Br₂, and the four carbons must be in a straight chain because the starting material was but-2-ene. From the integration, the four carbons must be present as one CH₃, one CH, and two CH₂ groups. The methyl is split into a doublet, so it must be adjacent to the CH. The two CH₂ groups must follow in succession, with two bromine atoms filling the remaining valences. (The spectrum is complex because the asymmetric carbon atom causes the neighboring protons to be diastereotopic.)



13-44 There is no evidence for vinyl hydrogens, so the compound must be a small, saturated, oxygen-containing molecule. Starting upfield (toward TMS), the first signal is a 3H triplet; this must be a CH₃ next to a CH₂. The CH₂ could be the signal at δ 1.5, but it has six peaks: it must have five neighboring hydrogens, a CH₃ on one side and a CH₂ on the other side. The third carbon must therefore be a CH₂; its signal is a quartet at δ 3.6, split by a CH₂ and an OH. To be so far downfield, the final CH₂ must be bonded to oxygen. The remaining 1H signal must be from an OH. The compound must be propan-1-ol.



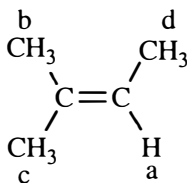
13-45



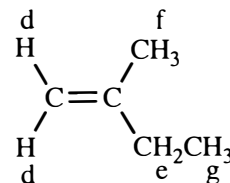
Isomer A

Isomer B

(a)



Isomer A



Isomer B

a = δ 5.2 (quartet, 1H)
 b = δ 1.7 (singlet, 3H)
 c = δ 1.6 (singlet, 3H)
 d = δ 1.5 (doublet, 3H)

d = δ 4.7 (singlet, 2H)
 e = δ 2.0 (quartet, 2H)
 f = δ 1.7 (singlet, 3H)
 g = δ 1.0 (triplet, 3H)

(b) With NaOH as base, the more highly substituted alkene, Isomer A, would be expected to predominate—the Zaitsev Rule. With KO-*t*-Bu as a hindered, bulky base, the less substituted alkene, Isomer B, would predominate (the Hofmann product).

13-46 "Nuclear waste" is comprised of radioactive products from either nuclear reactions, for example, from electrical generating stations powered by nuclear reactors, or residue from medical or scientific studies using radioactive nuclides as therapeutic agents (like iodine for thyroid treatment) or as molecular tracers (carbon-14, tritium H-3, phosphorus-32, nitrogen-15, and many others). The physical technique of *nuclear* magnetic resonance neither uses nor generates any radioactive elements, and does not generate "nuclear waste". (Some people assume that the medical application of NMR, medical resonance imaging or MRI, purposely dropped the word "nuclear" from the technique to avoid the confusion between "nuclear" and "radioactive".)

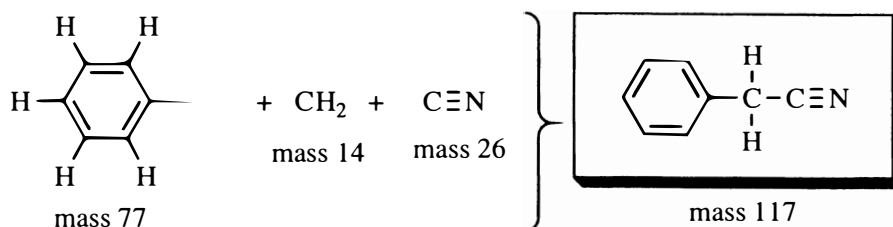
13-47

Mass spectrum: The molecular ion of m/z 117 suggests the presence of an odd number of nitrogens.

Infrared spectrum: No NH or OH appears. Hydrogens bonded to both sp^2 and sp^3 carbon are indicated around 3000 cm^{-1} . The characteristic $\text{C}\equiv\text{N}$ peak appears at 2250 cm^{-1} and aromatic $\text{C}=\text{C}$ is suggested by the peak at 1600 cm^{-1} .

NMR spectrum: Five aromatic protons are shown in the NMR at δ 7.3. A CH_2 singlet appears at δ 3.7.

Assemble the pieces:



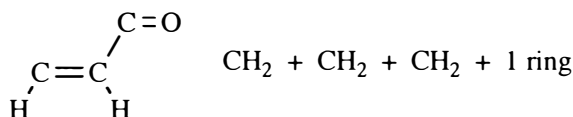
13-48 This is a challenging problem, despite the molecule being relatively small.

Mass spectrum: The molecular ion at 96 suggests no Cl, Br, or N. The molecule must have seven carbons or fewer.

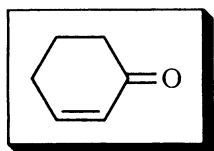
Infrared spectrum: The dominant functional group peak is at 1685 cm^{-1} , a carbonyl that is conjugated with C=C (lower wavenumber than normal, very intense peak). The presence of an oxygen and a molecular ion of 96 lead to a formula of $\text{C}_6\text{H}_8\text{O}$, with three elements of unsaturation, a C=O and one or two C=C.

Carbon NMR spectrum: The six peaks show, by chemical shift, one carbonyl carbon (196), two alkene carbons (129, 151), and three aliphatic carbons (23, 26, 36). By off-resonance decoupling multiplicity, the groups are: three CH_2 groups, two alkene CH groups, and carbonyl.

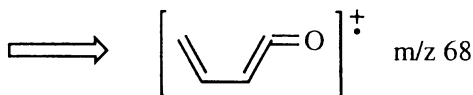
Since the structure has one carbonyl and only two alkene carbons, the third element of unsaturation must be a ring.



Since the structure has no methyl group, and no $\text{H}_2\text{C}=\text{}$, all of the carbons must be included in the ring. The only way these pieces can fit together is in cyclohex-2-enone. Notice that the proton NMR was unnecessary to determine the structure, fortunately, since the HNMR was not easily interpreted except for the two alkene hydrogens; the hydrogen on carbon-2 appears as the doublet at 6.0.

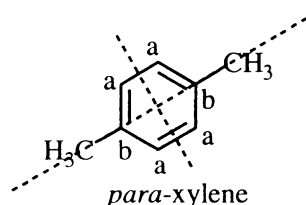
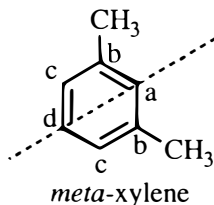
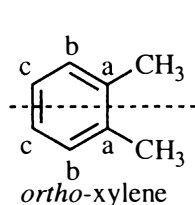


cyclohex-2-enone



The mystery mass spec peak at $m/z \ 68$ comes from a fragmentation that will be discussed later; it is called a retro-Diels-Alder fragmentation.

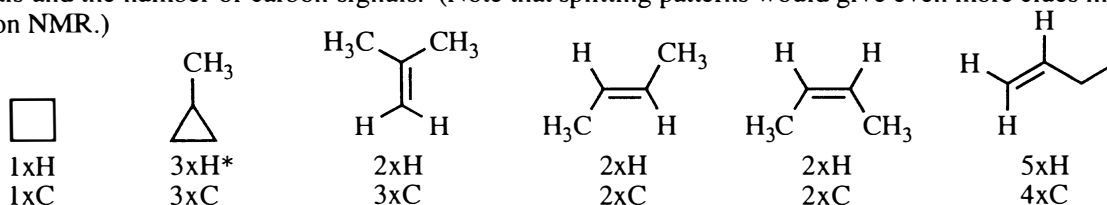
13-49 The key to the carbon NMR lies in the symmetry of these structures.



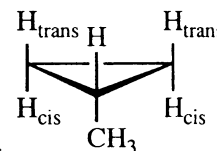
(a) In each molecule, the methyl carbons are equivalent, giving one signal in the CNMR. Considering the ring carbons, the symmetry of the structures shows that *ortho*-xylene would have 3 carbon signals from the ring (total of 4 peaks), *meta*-xylene would have 4 carbon signals from the ring (total of 5 peaks), and *para*-xylene would have only 2 carbon signals from the ring (total of 3 peaks). These compounds would be instantly identifiable simply by the number of peaks in the carbon NMR.

(b) The proton NMR would be a completely different problem. Unless the substituent on the benzene ring is moderately electron-withdrawing or donating, the ring protons absorb at roughly the same position. A methyl group has essentially no electronic effect on the ring hydrogens, so while the *para* isomer would give a clean singlet because all its ring protons are equivalent, the *ortho* and *meta* isomers would have only slightly broadened singlets for their proton signals. (Only a very high field NMR, 500 MHz or higher, would be able to distinguish these isomers in the proton NMR.)

13-50 (a), (b) and (c) The six isomers are drawn here. Below each structure is the number of proton signals and the number of carbon signals. (Note that splitting patterns would give even more clues in the proton NMR.)

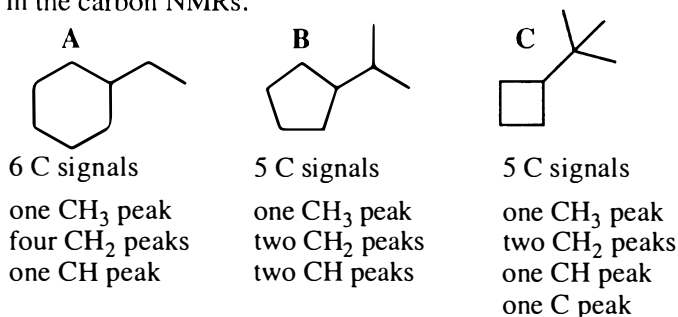


*Rings always present challenges in stereochemistry. When viewed in three dimensions, it becomes apparent that the two hydrogens on a CH₂ are not equivalent: on each CH₂, one H is cis to the methyl and one H is trans to the methyl. These are diastereotopic protons. A more correct answer to part (b) would be four types of protons; whether all four could be distinguished in the NMR is a harder question to answer. For the purpose of this problem, whether it is 3 or 4 types of H does not matter because either one, in combination with three types of carbon, will distinguish it from the other 5 structures.



(d) Two types of H and three types of C can be only one isomer: 2-methylpropene (isobutylene). (The only isomers that would not be distinguished from each other would be *cis*- and *trans*-but-2-ene.)

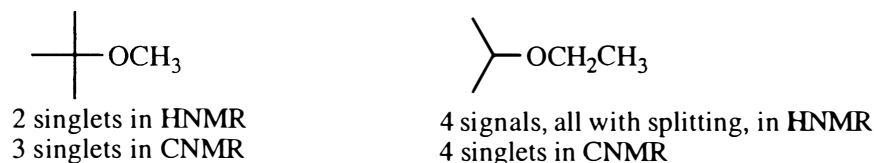
13-51 For DEPT to be useful in distinguishing isomers, there should be different numbers of CH₃, CH₂, CH, and C signals in the carbon NMRs.



A carbon NMR could not distinguish isomers **B** and **C**, and if there is any overlap in the signals, it might have a difficult time distinguishing **A**. Fortunately, the patterns that would appear in the DEPT-90 would distinguish **B** (two CH peaks up) from the other two (1 CH peak up), and the DEPT-135 would instantly distinguish **A** (4 CH₂ peaks down) from **C** (2 CH₂ peaks down).

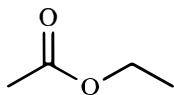
13-52

(a) MS or IR could not easily distinguish these isomers: same molecular weight and same functional group. They would give dramatically different proton and carbon NMRs however.



13-52 continued

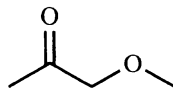
(b) The only technique that would not readily distinguish these isomers would be MS because they have the same molecular weight and would have similar, though not identical, fragmentation patterns.



IR: C=O about 1730 cm^{-1}

¹H NMR: methyl singlet and ethyl pattern

¹³C NMR: ester C=O about δ 170

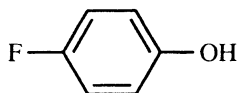


IR: C=O about 1710 cm^{-1}

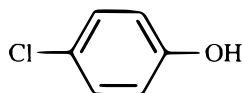
¹H NMR: 3 singlets

¹³C NMR: ketone C=O about δ 200

(c) The big winner here is MS: they have different molecular weights, plus the Cl has the two isotope peaks that make a Cl atom easily distinguished. The other techniques would have minor differences and would require having a detailed table of frequencies or chemical shifts to determine which is which.



$M^+ = m/z$ 112



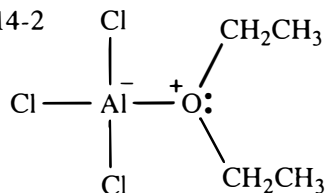
$M^+ = m/z$ 128, 130

CHAPTER 14—ETHERS, EPOXIDES AND SULFIDES

14-1

The four solvents decrease in polarity in this order: water, ethanol, ethyl ether, and dichloromethane. The three solutes decrease in polarity in this order: sodium acetate, 2-naphthol, and naphthalene. The guiding principle in determining solubility is, "Like dissolves like." Compounds of similar polarity will dissolve (in) each other. Thus, sodium acetate will dissolve in water, will dissolve only slightly in ethanol, and will be virtually insoluble in ethyl ether and dichloromethane. 2-Naphthol will be insoluble in water, somewhat soluble in ethanol, and soluble in ether and dichloromethane. Naphthalene will be insoluble in water, partially soluble in ethanol, and soluble in ethyl ether and dichloromethane. (Actual solubilities are difficult to predict, but you should be able to predict *trends*.)

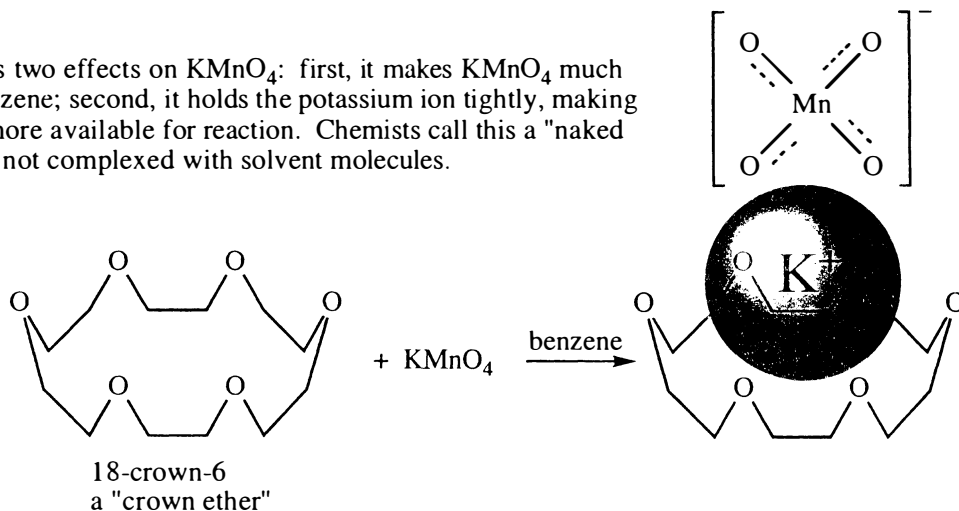
14-2



Oxygen shares one of its electron pairs with aluminum; oxygen is the Lewis base, and aluminum is the Lewis acid. An oxygen atom with three bonds and one unshared pair has a positive formal charge. An aluminum atom with four bonds has a negative formal charge.

14-3

The crown ether has two effects on KMnO_4 : first, it makes KMnO_4 much more soluble in benzene; second, it holds the potassium ion tightly, making the permanganate more available for reaction. Chemists call this a "naked anion" because it is not complexed with solvent molecules.

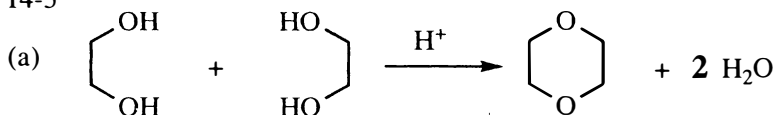


Please see the note on p. 13 of this Solutions Manual regarding placement of position numbers.

14-4 IUPAC name first; then common name (see Appendix 1 in this Solutions Manual for a summary of IUPAC nomenclature)

- (a) methoxycyclopropane; cyclopropyl methyl ether
- (b) 2-ethoxypropane; ethyl isopropyl ether
- (c) 1-chloro-2-methoxyethane; 2-chloroethyl methyl ether
- (d) 2-ethoxy-2,3-dimethylpentane; no common name
- (e) 2-*t*-butoxybutane; *sec*-butyl *t*-butyl ether
- (f) *trans*-2-methoxycyclohexan-1-ol; no common name

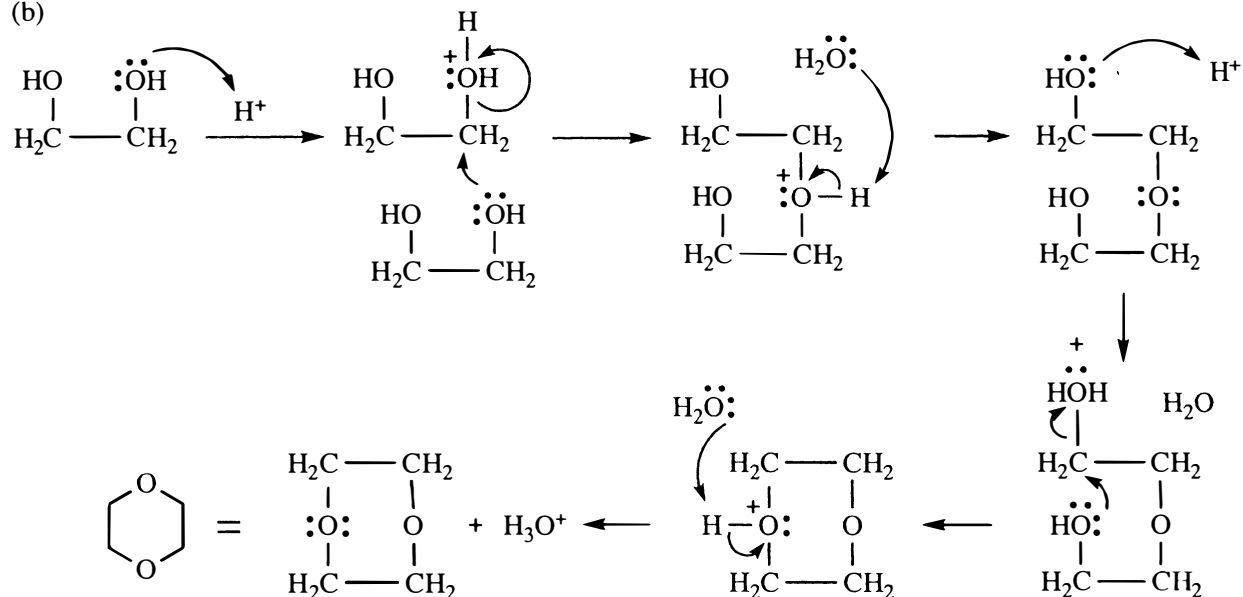
14-5



The alcohol is ethane-1,2-diol; the common name is ethylene glycol.

14-5 continued

(b)

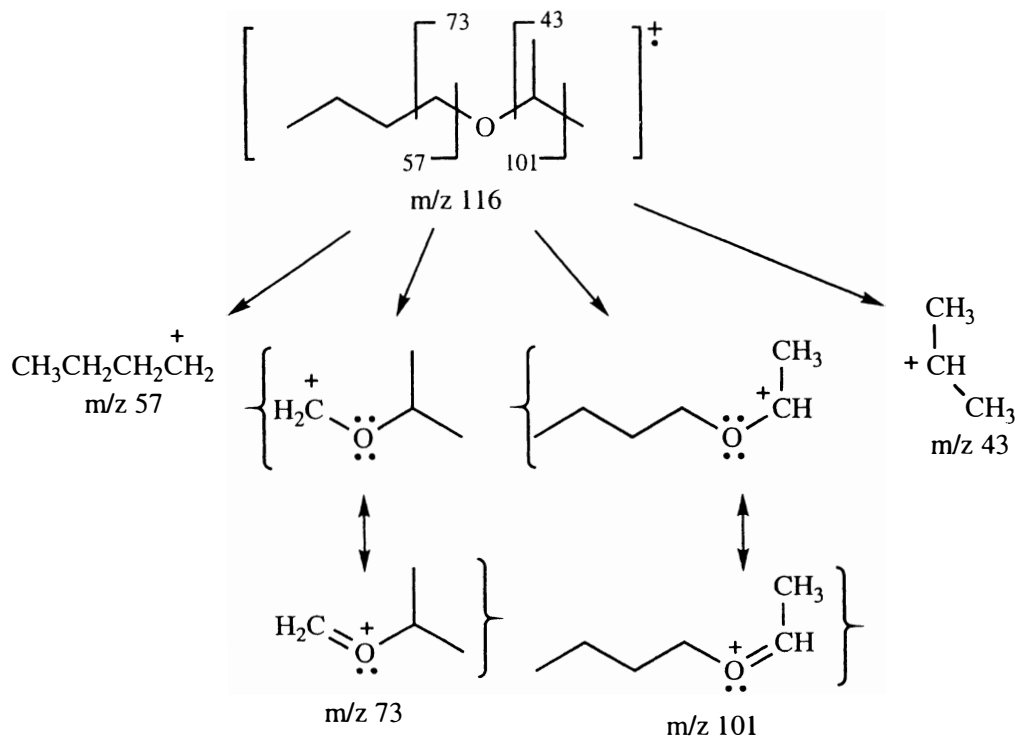


The mechanism shows that the acid catalyst is regenerated at the end of the reaction.

14-6

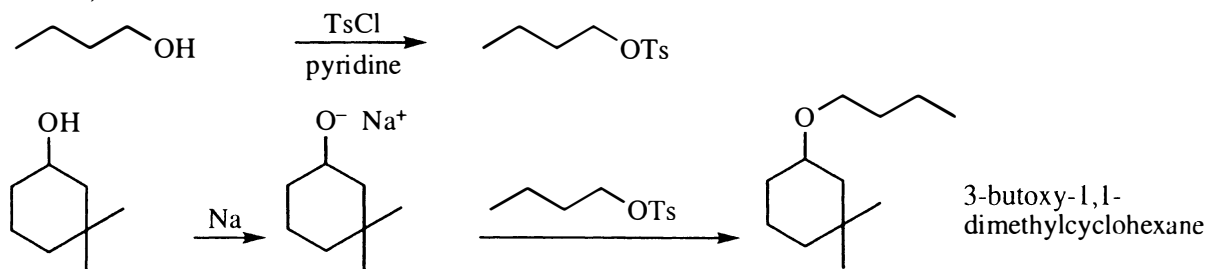
- (a) dihydropyran
 (b) 2-chloro-1,4-dioxane
 (c) 3-isopropylpyran
 (d) *trans*-2,3-diethyloxirane; *trans*-3,4-epoxyhexane; *trans*-3-hexene oxide
 (e) 3-bromo-2-ethoxyfuran
 (f) 3-bromo-2,2-dimethyloxetane

14-7

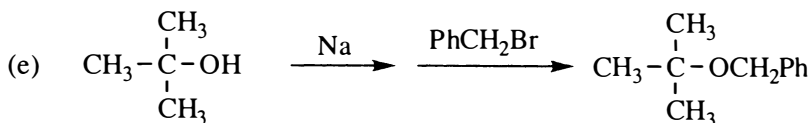
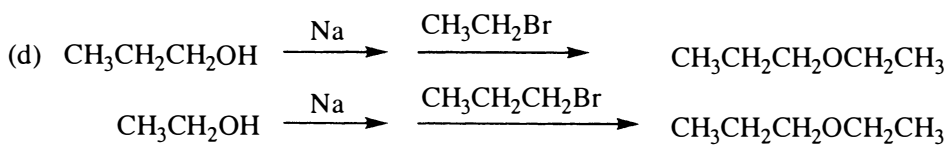
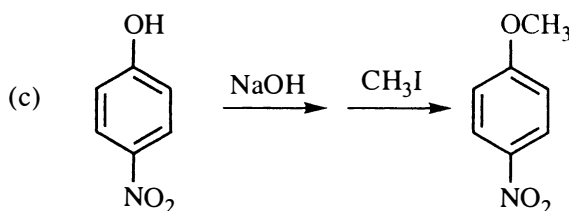
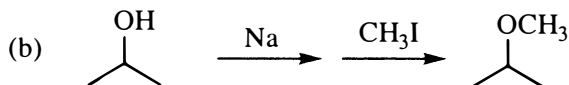
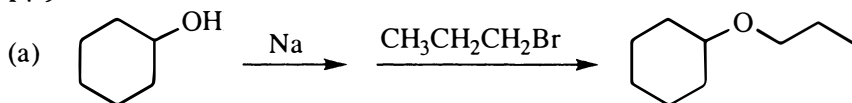


14-8 S_N2 reactions, including the Williamson ether synthesis, work best when the nucleophile attacks a 1° or methyl carbon. Instead of attempting to form the bond from oxygen to the 2° carbon on the ring, form the bond from oxygen to the 1° carbon of the butyl group.

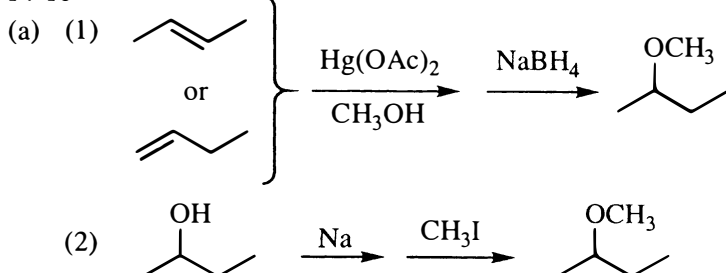
The OH must first be transformed into a good leaving group: either a tosylate, or one of the halides (not fluoride).



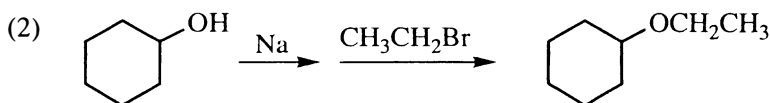
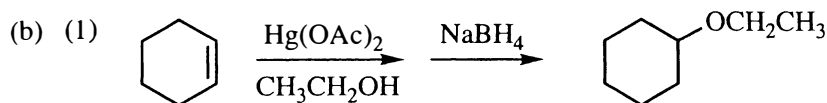
14-9



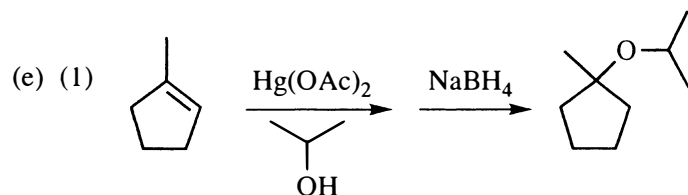
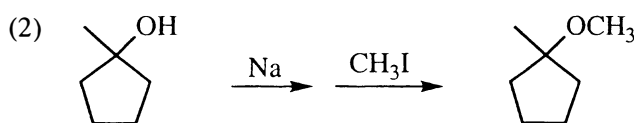
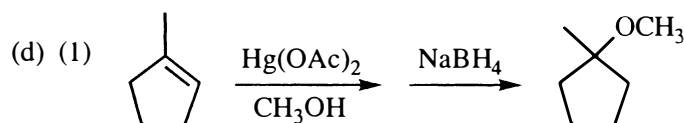
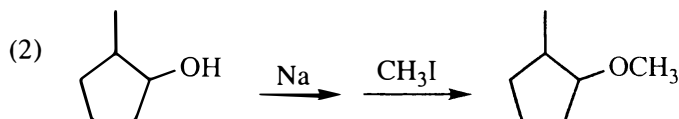
14-10



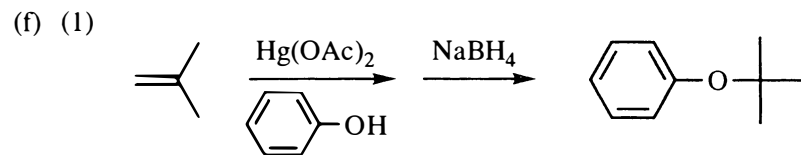
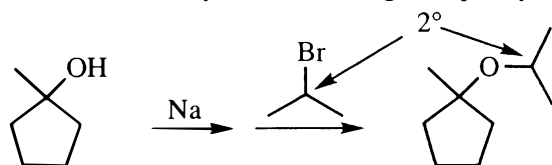
14-10 continued



(c) (1) Alkoxymercuration is not practical here; the product does not have Markovnikov orientation.



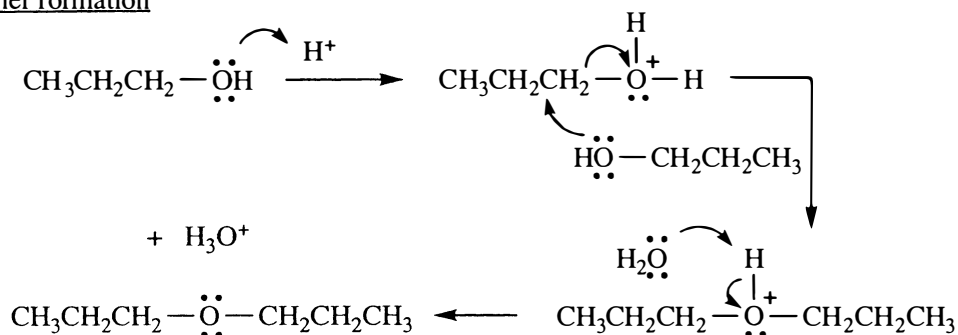
(2) Williamson ether synthesis would give a poor yield of product as the halide is on a 2° carbon.



(2) Williamson ether synthesis is not feasible here. S_N2 does not work on either a benzene or a 3° halide.

14-11 An important principle of synthesis is to avoid mixtures of isomers wherever possible; minimizing separations increases recovery of products. Bimolecular dehydration is a random process. Heating a mixture of ethanol and methanol with acid will produce all possible combinations: dimethyl ether, ethyl methyl ether, and diethyl ether. This mixture would be troublesome to separate.

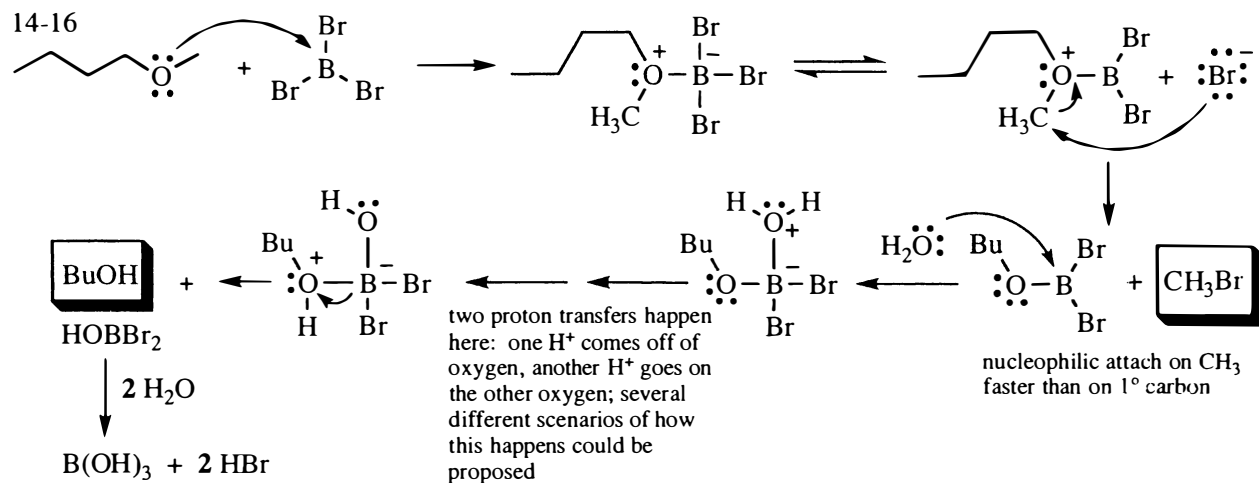
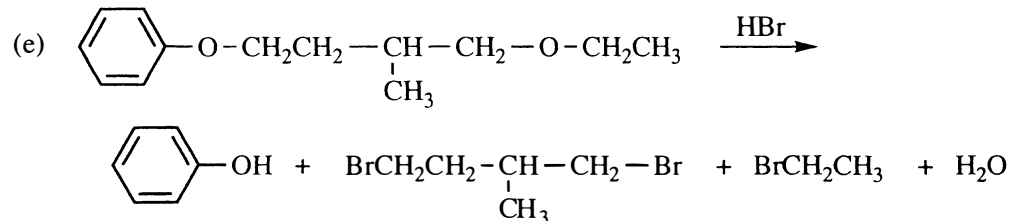
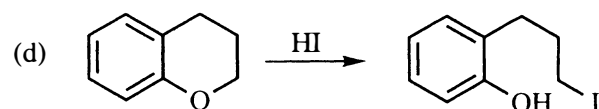
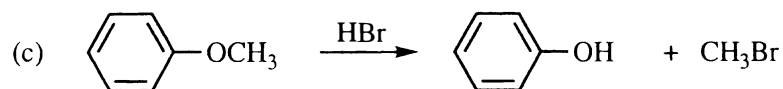
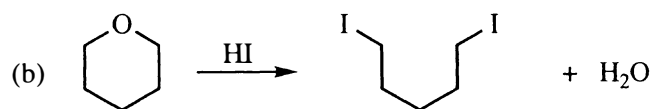
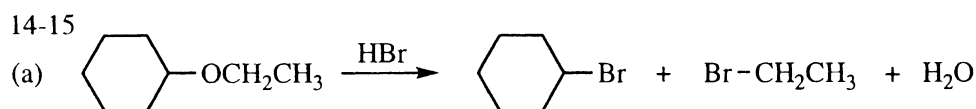
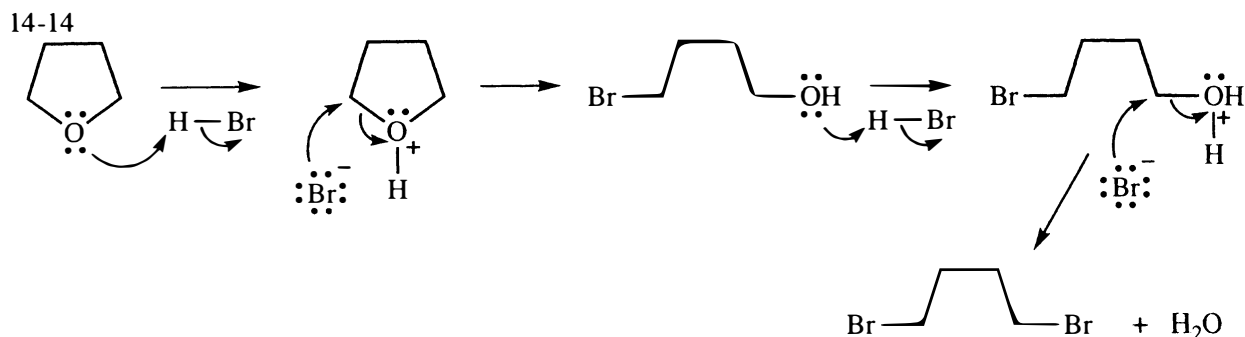
Ether formation


$$\text{CH}_3\text{CH}_2\text{CH}_2-\ddot{\text{O}}\text{H} \xrightarrow{\text{H}^+} \text{CH}_3\underset{\text{H}}{\text{CH}}\text{CH}_2-\overset{\text{H}}{\underset{\cdot\cdot}{\text{O}}}^+-\text{H} \xrightarrow{\text{H}_2\ddot{\text{O}}} \text{CH}_3\text{CH}=\text{CH}_2 + \text{H}_2\text{O}$$

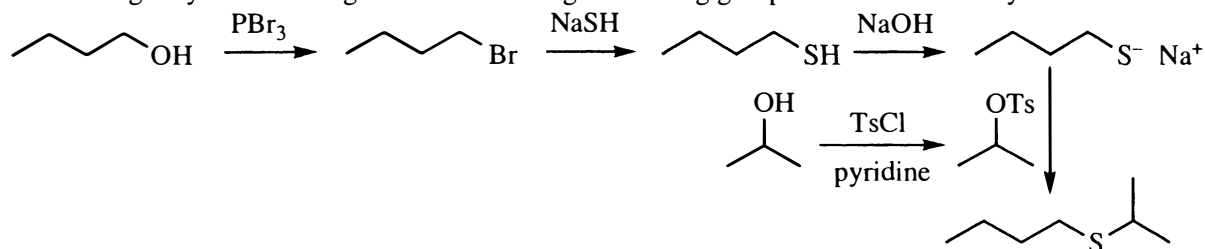
14-13

- $$\begin{array}{ccccc} \text{CH}_3\text{CH}_2\text{OH} & \xrightarrow{\text{Na}} & \xrightarrow{\text{CH}_3\text{CH}_2\text{Br}} & & \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3 \\ \text{CH}_3\text{CH}_2\text{OH} & \xrightarrow{\text{Na}} & \xrightarrow{\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}} & & \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_3 \end{array}$$

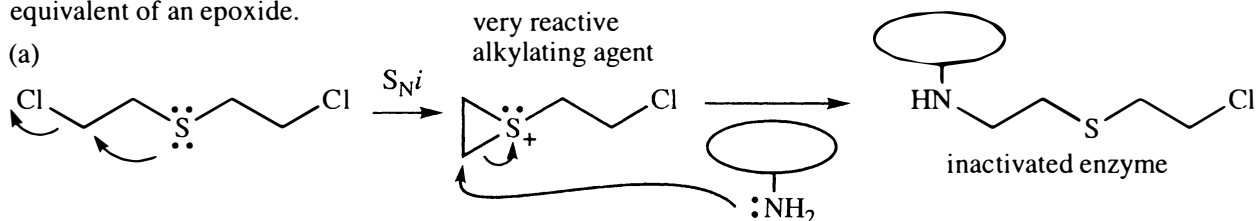
- CC=CC + CC=CC >> CC(O)CC >> CC(OC(C)C)CC



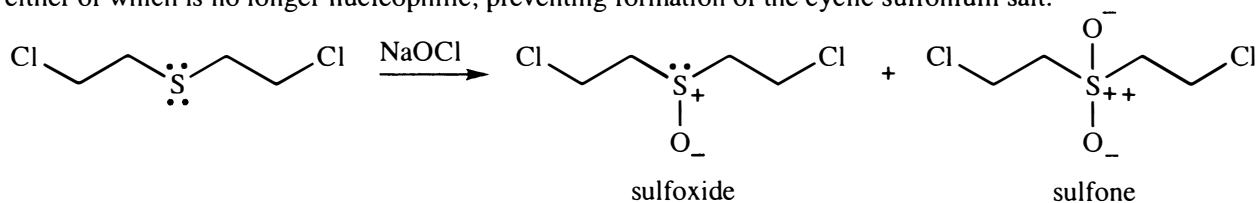
14-17 Begin by transforming the alcohols into good leaving groups like halides or tosylates:



14-18 The sulfur at the center of mustard gas is an excellent nucleophile, and chloride is a decent leaving group. Sulfur can do *internal* nucleophilic substitution to make a reactive sulfonium salt and the sulfur equivalent of an epoxide.

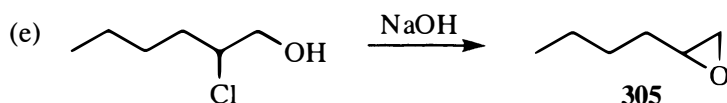
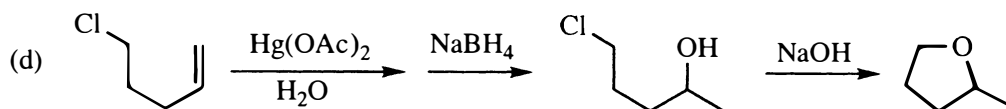
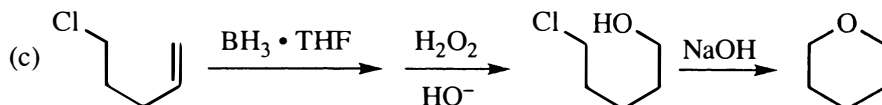
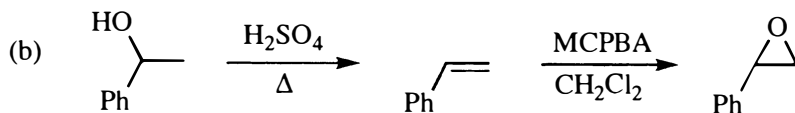
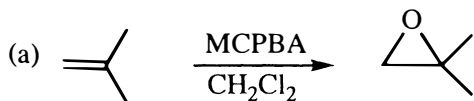


(b) NaOCl is a powerful oxidizing agent. It oxidizes sulfur to a sulfoxide or more likely a sulfone, either of which is no longer nucleophilic, preventing formation of the cyclic sulfonium salt.



14-19

Generally, chemists prefer the peroxyacid method of epoxide formation to the halohydrin method. Reactions (a) and (b) show the peroxyacid method, but the halohydrin method could also be used.

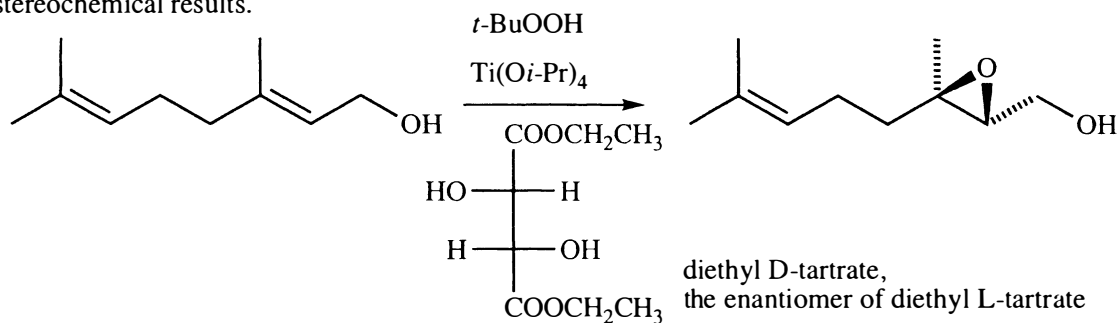


14-20

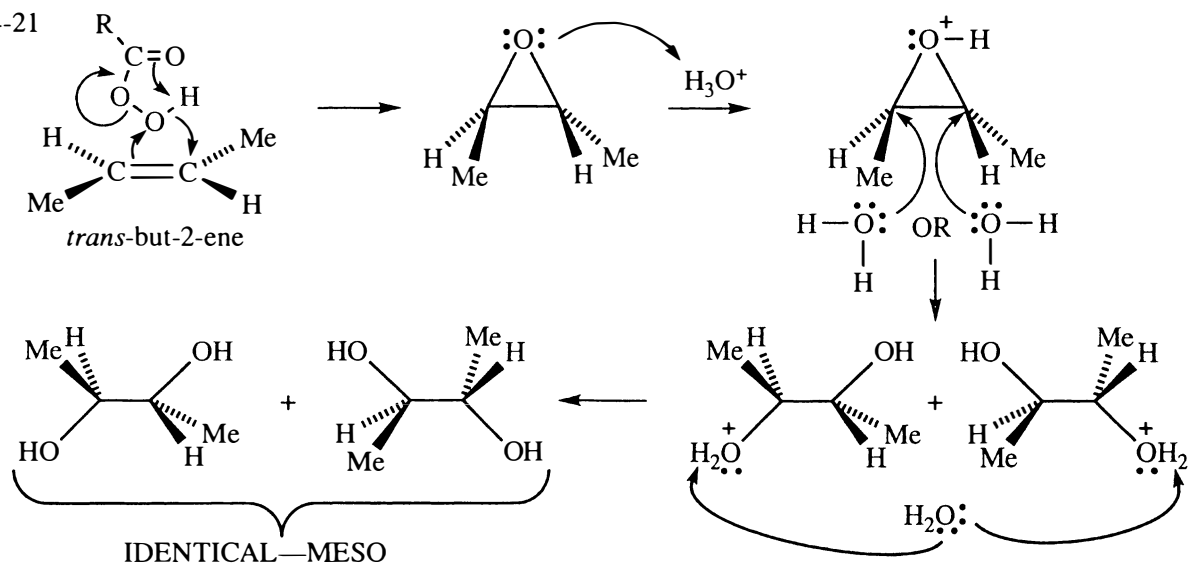
(a) 1) *tert*-Butyl hydroperoxide is the oxidizing agent. The $(\text{CH}_3)_3\text{COOH}$ contains the O—O bond just like a peroxyacid. 2) Diethyl tartrate has two asymmetric carbons and is the source of asymmetry; its function is to create a chiral transition state that is of lowest energy, leading to only one enantiomer of product. This process is called *chirality transfer*. 3) The function of the titanium (IV) isopropoxide is to act as the glue that holds all of the reagents together. The titanium holds an oxygen from each reactant—geraniol, *t*-BuOOH, and diethyl tartrate—and tethers them so that they react together, rather than just having them in solution and hoping that they will eventually collide.

(b) All three reactants are required to make Sharpless epoxidation work, but the key to *enantioselective* epoxidation is the chiral molecule, diethyl tartrate. When it complexes (or *chelates*) with titanium, it forms a large structure that is also chiral. As the *t*-BuOOH and geraniol approach the complex, the steric requirements of the complex allow the approach in one preferred orientation. When the reaction between the alkene and *t*-BuOOH occurs, it occurs preferentially from one face of the alkene, leading to one major stereoisomer of the epoxide. Without the chiral diethyl tartrate in the complex, the alkene could approach from one side just as easily as the other, and a racemic mixture would be formed.

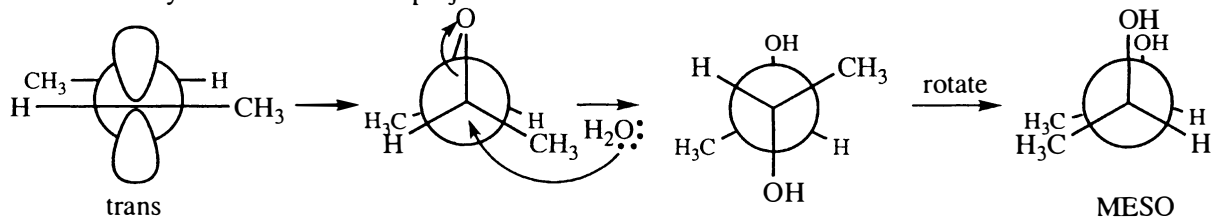
(c) Using the enantiomer of diethyl L-tartrate, called diethyl D-tartrate, would give exactly the opposite stereochemical results.



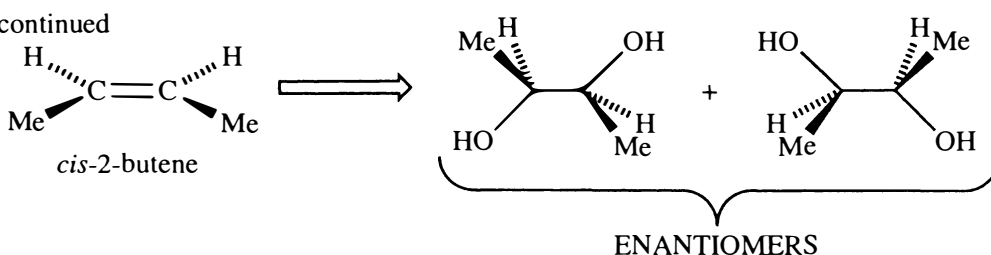
14-21



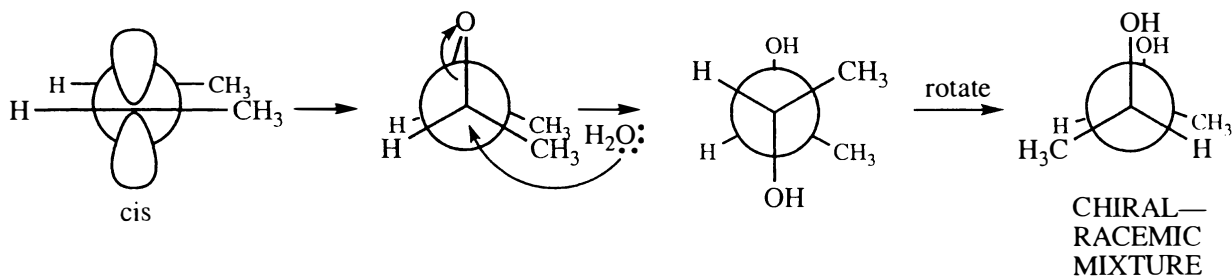
stereochemistry shown in Newman projections:



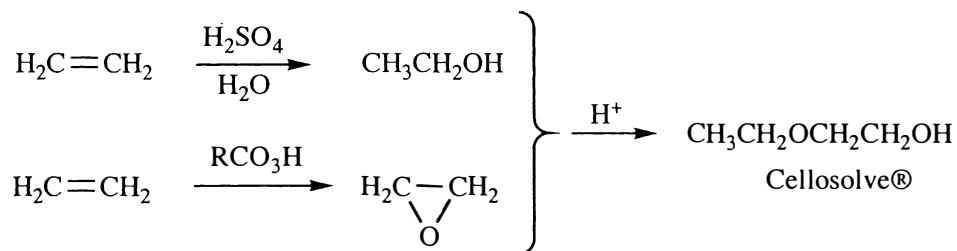
14-21 continued



stereochemistry shown in Newman projections:

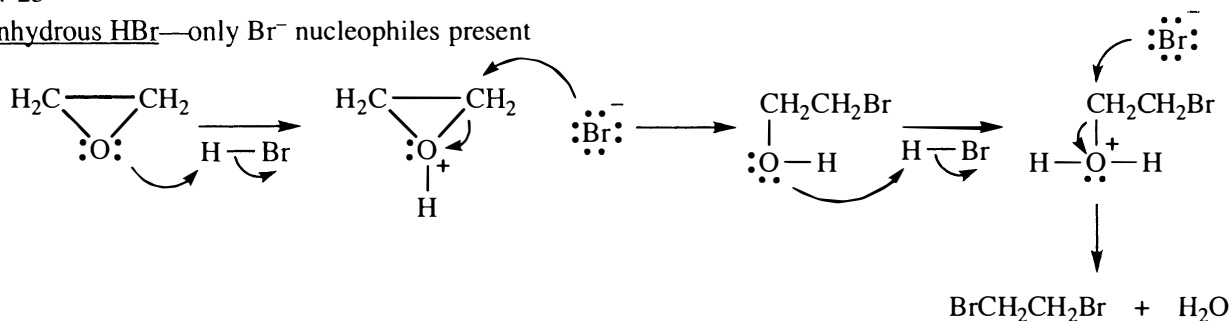


14-22

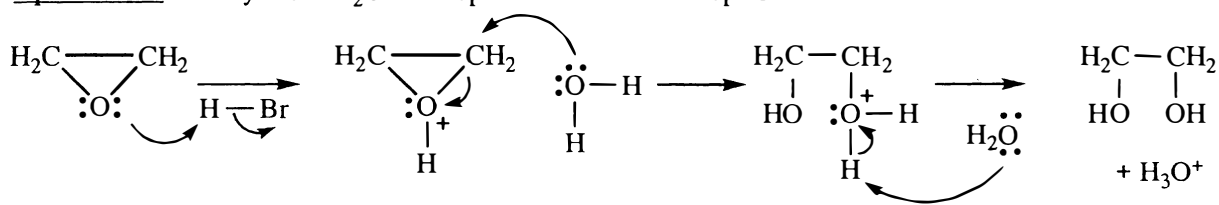


14-23

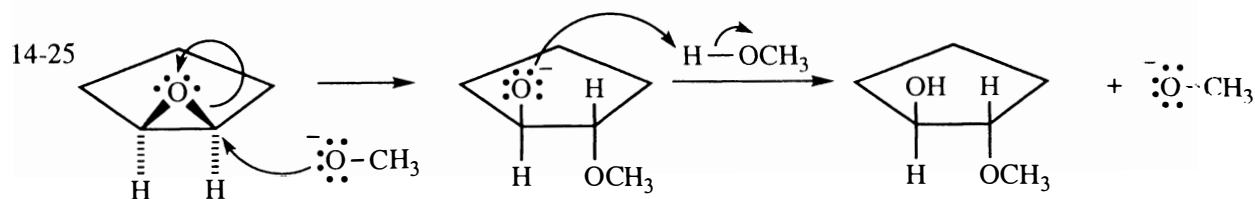
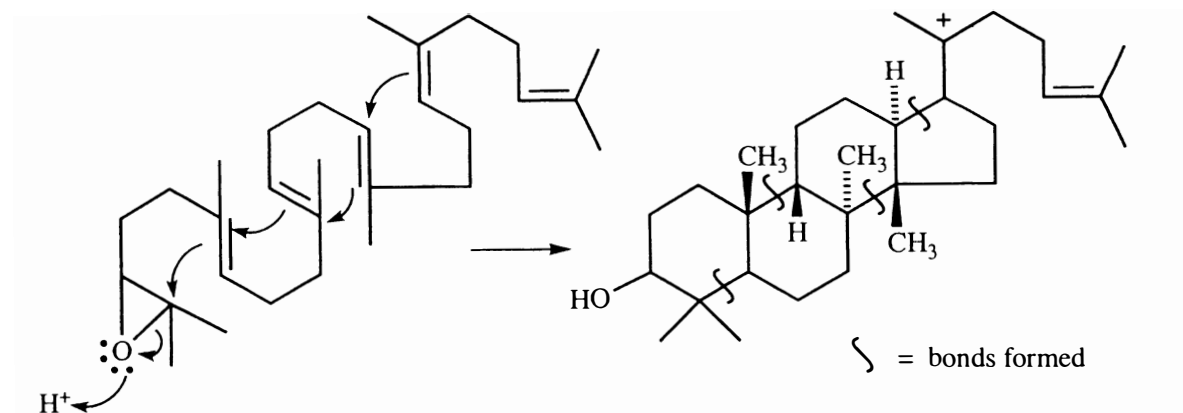
anhydrous HBr—only Br^- nucleophiles present



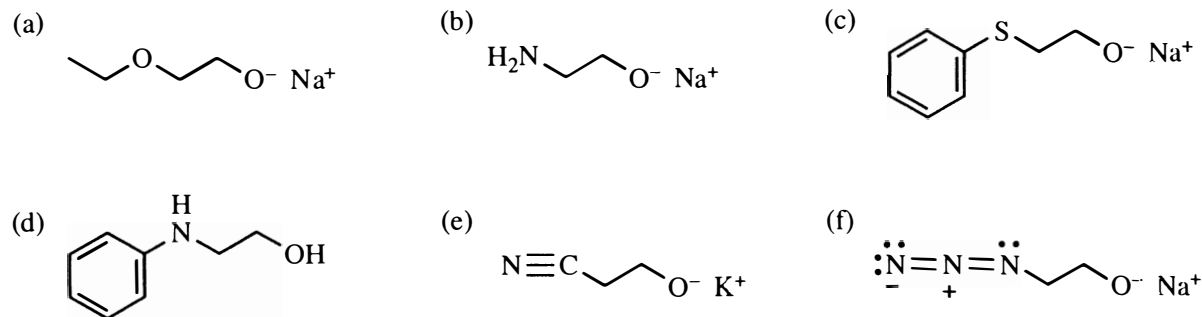
aqueous HBr—many more H_2O nucleophiles than Br^- nucleophiles



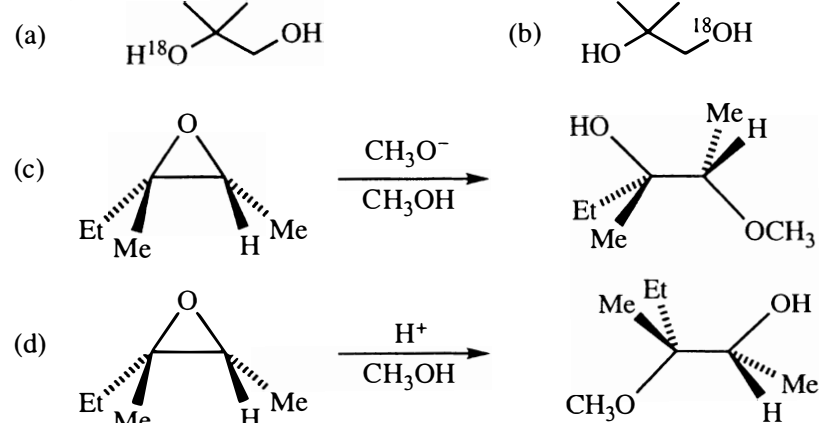
14-24 The cyclization of squalene via the epoxide is an excellent (and extraordinary) example of how Nature uses organic chemistry to its advantage. In one enzymatic step, Nature forms four rings and eight chiral centers! Out of 256 possible stereoisomers, only one is formed!



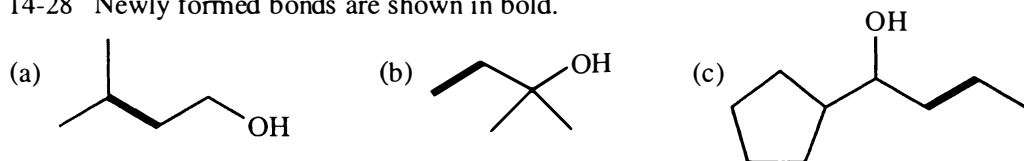
14-26



14-27

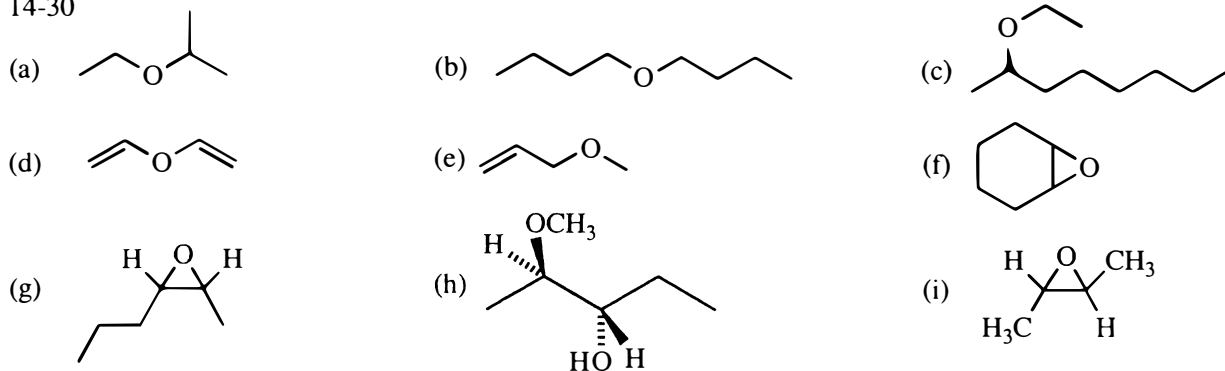


14-28 Newly formed bonds are shown in bold.



14-29 Please refer to solution 1-20, page 12 of this Solutions Manual.

14-30



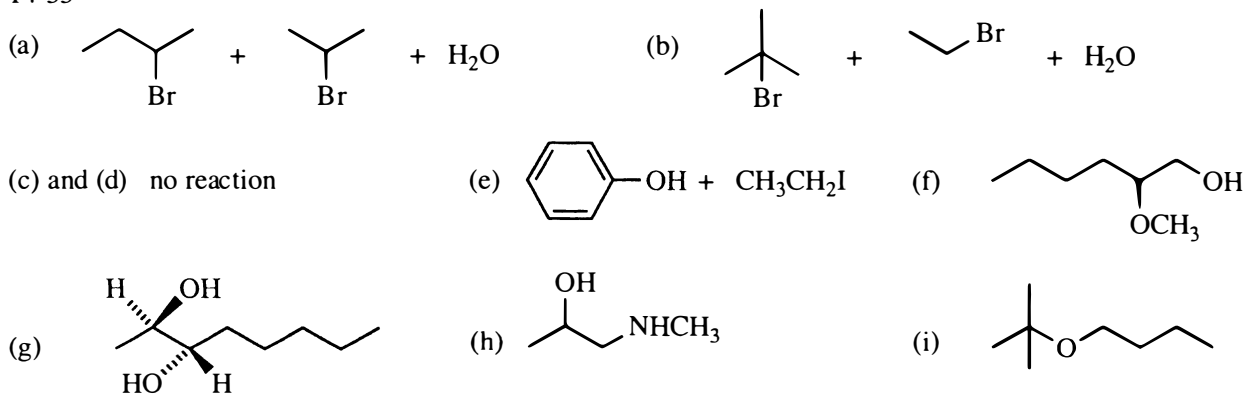
14-31

- (a) *sec*-butyl isopropyl ether
 (b) *t*-butyl isobutyl ether
 (c) ethyl phenyl ether
 (d) chloromethyl *n*-propyl ether
 (e) *trans*-cyclohexene glycol
 (f) cyclopentyl methyl ether
 (g) propylene oxide
 (h) cyclopentene oxide

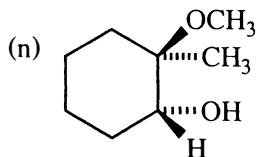
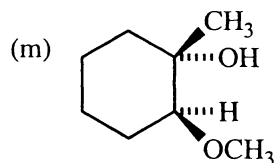
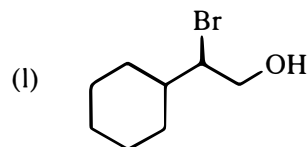
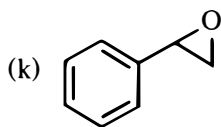
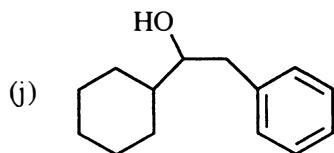
14-32

- (a) 2-methoxypropan-1-ol
 (b) ethoxybenzene or phenoxyethane
 (c) methoxycyclopentane
 (d) 2,2-dimethoxycyclopentan-1-ol
 (e) *trans*-1-methoxy-2-methylcyclohexane
 (f) *trans*-3-chloro-1,2-epoxycycloheptane
 (g) *trans*-1-methoxy-1,2-epoxybutane; or, *trans*-2-ethyl-3-methoxyoxirane
 (h) 3-bromooxetane
 (i) 1,3-dioxane

14-33



14-33 continued



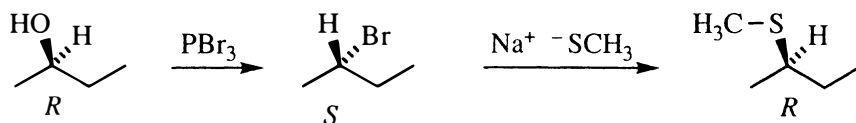
14-34

(a) On long-term exposure to air, ethers form peroxides. Peroxides are explosive when concentrated or heated. (For exactly this reason, ethers should *never* be distilled to dryness.)

(b) Peroxide formation can be prevented by excluding oxygen. Ethers can be checked for the presence of peroxides, and peroxides can be destroyed safely by treatment with reducing agents.

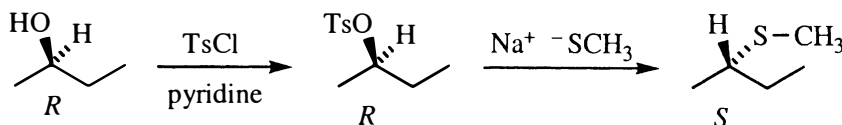
14-35

(a) Beginning with (*R*)-butan-2-ol and producing the (*R*) sulfide requires two inversions of configuration.

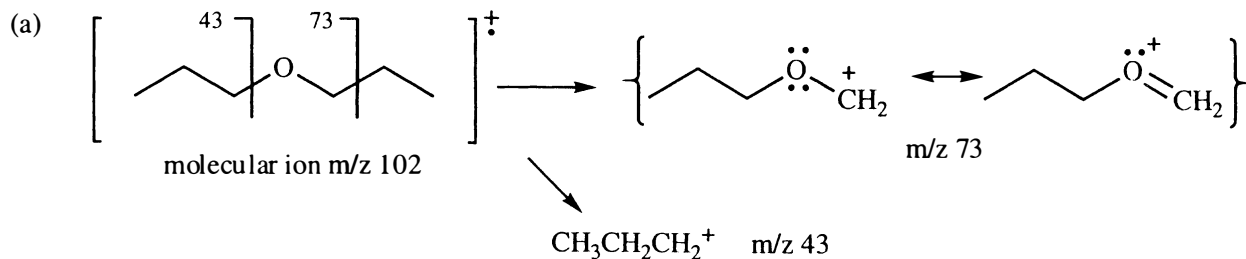


An alternative approach would be to make the tosylate, displace with chloride or bromide (S_N2 with inversion), then do a second inversion with NaSCH_3 .

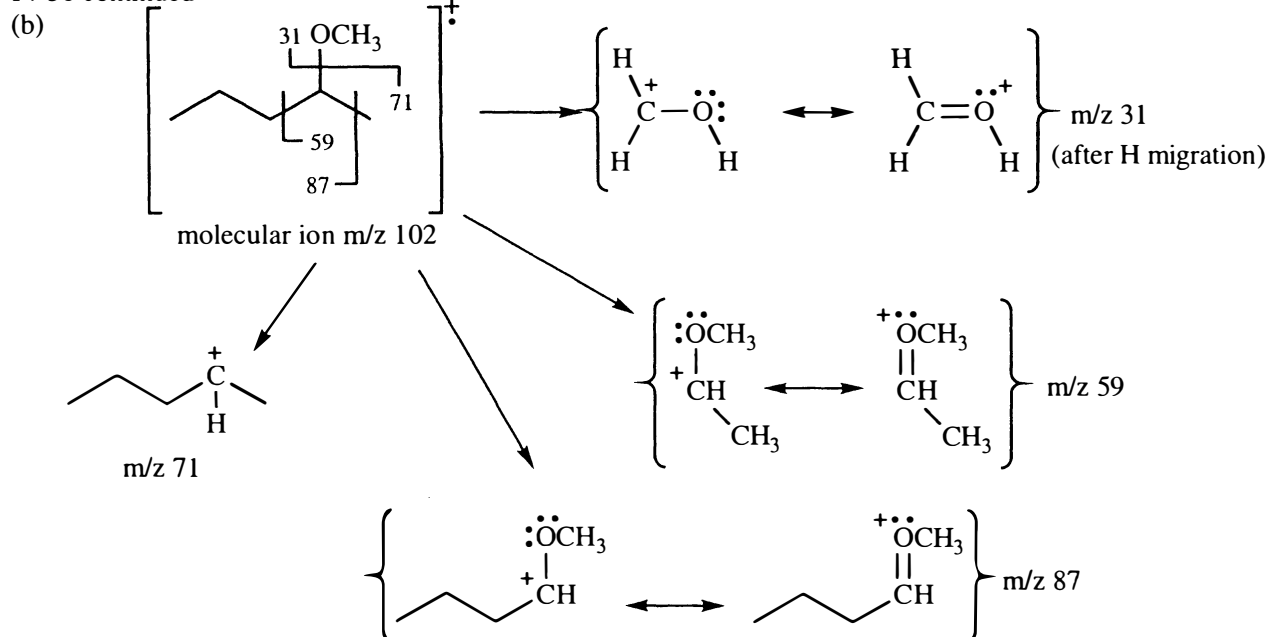
(b) Synthesis of the (*S*) isomer directly requires only one inversion.



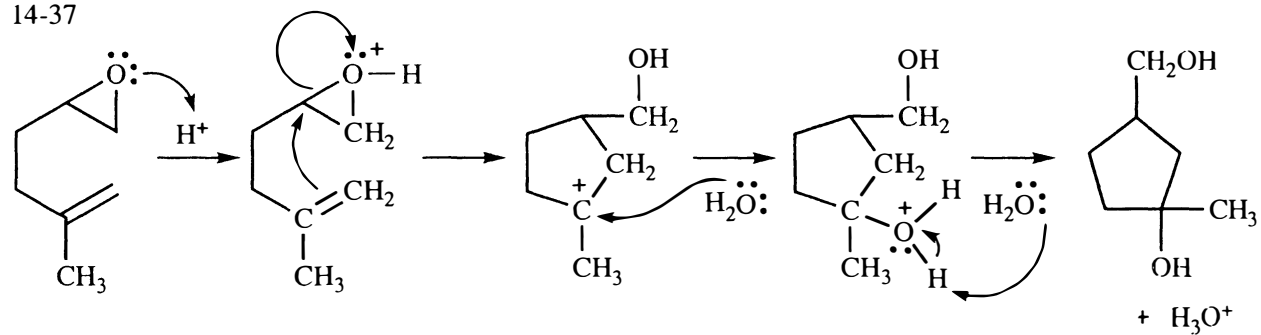
14-36



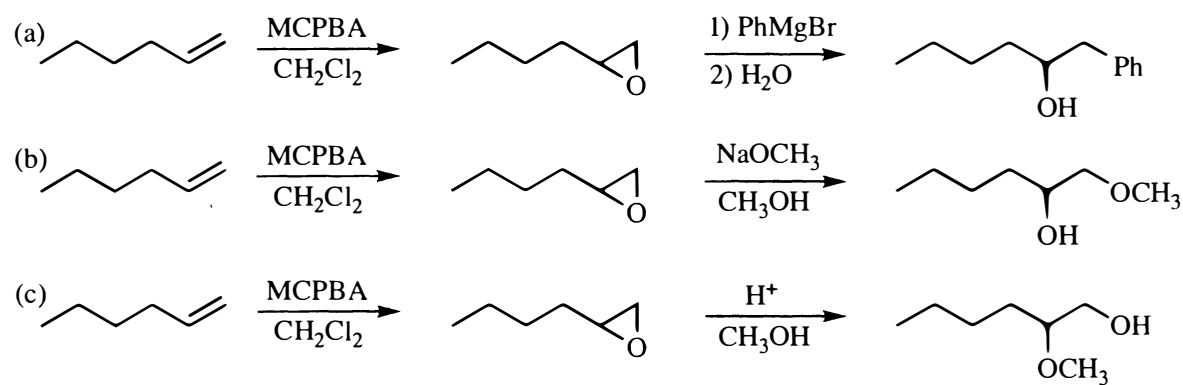
14-36 continued

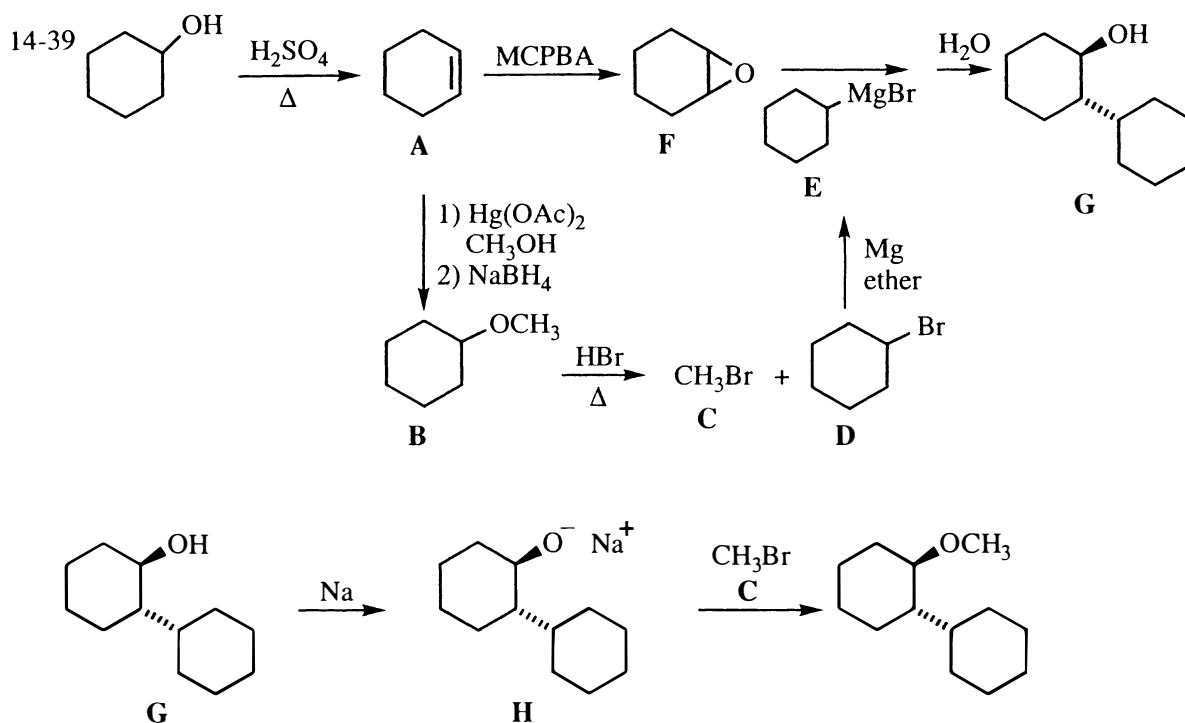


14-37



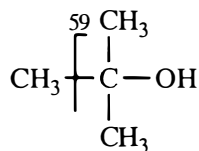
14-38





14-40 The student turned in the wrong product! Three pieces of information are consistent with the desired product: molecular formula $\text{C}_4\text{H}_{10}\text{O}$; O—H stretch in the IR at 3300 cm^{-1} (although it should be strong, not weak); and mass spectrum fragment at m/z 59 (loss of CH_3). The NMR of the product should have a 9H singlet at δ 1.0 and a 1H singlet between δ 2 and δ 5. Instead, the NMR shows CH_3CH_2 bonded to oxygen. The student isolated diethyl ether, the typical solvent used in Grignard reactions.

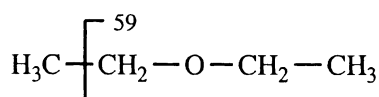
Predicted product



$\text{C}_4\text{H}_{10}\text{O}$

O—H at 3300 cm^{-1}

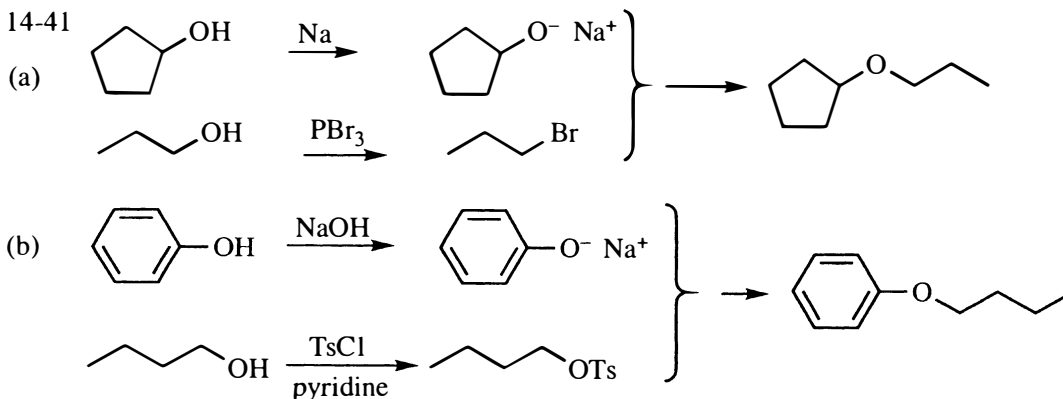
Isolated product



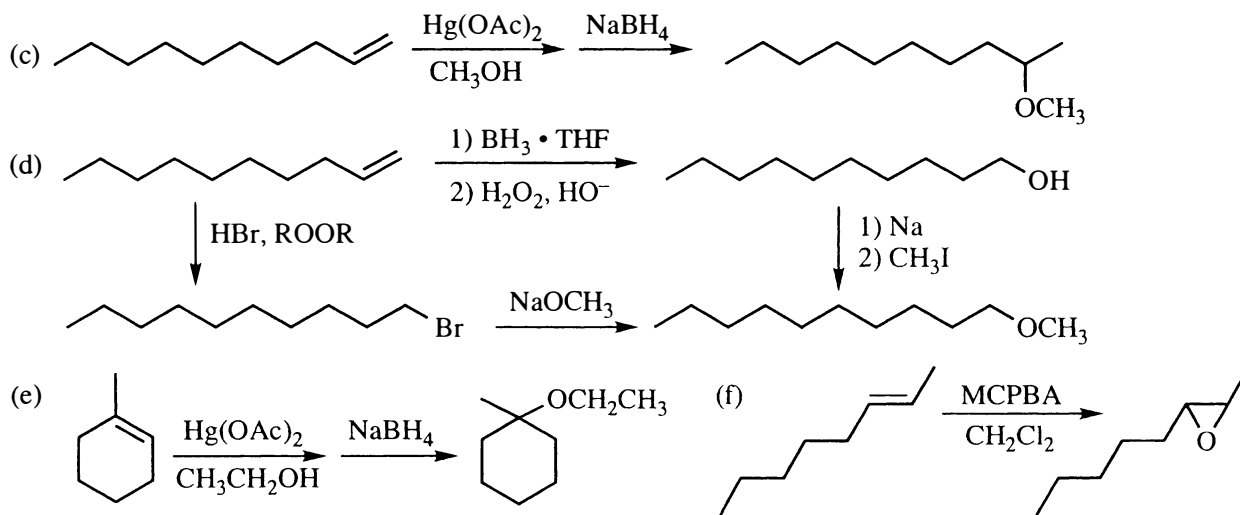
$\text{C}_4\text{H}_{10}\text{O}$

O—H at 3300 cm^{-1} due to water contamination

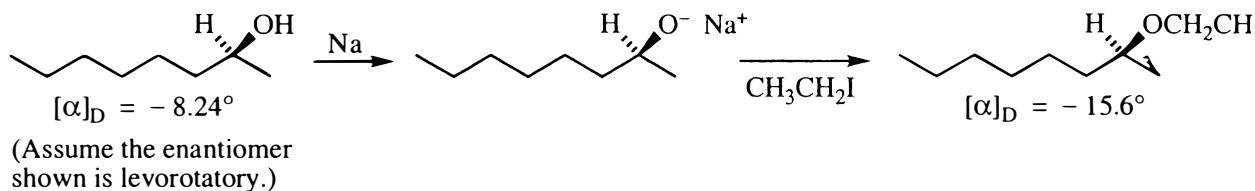
14-41



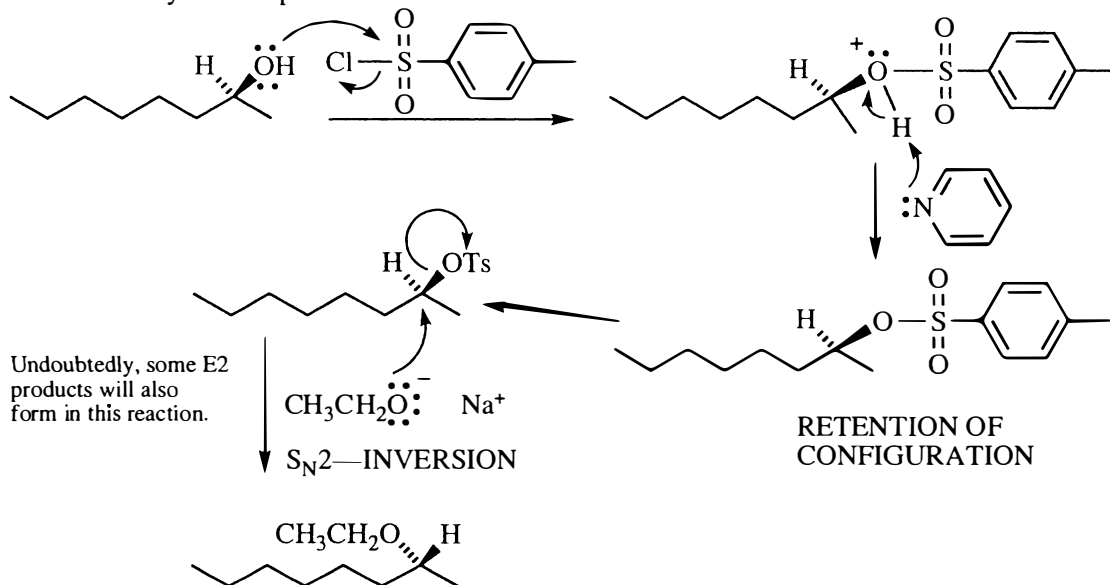
14-41 continued



14-42 In the first sequence, no bond is broken to the chiral center, so the configuration of the product is the same as the configuration of the starting material.

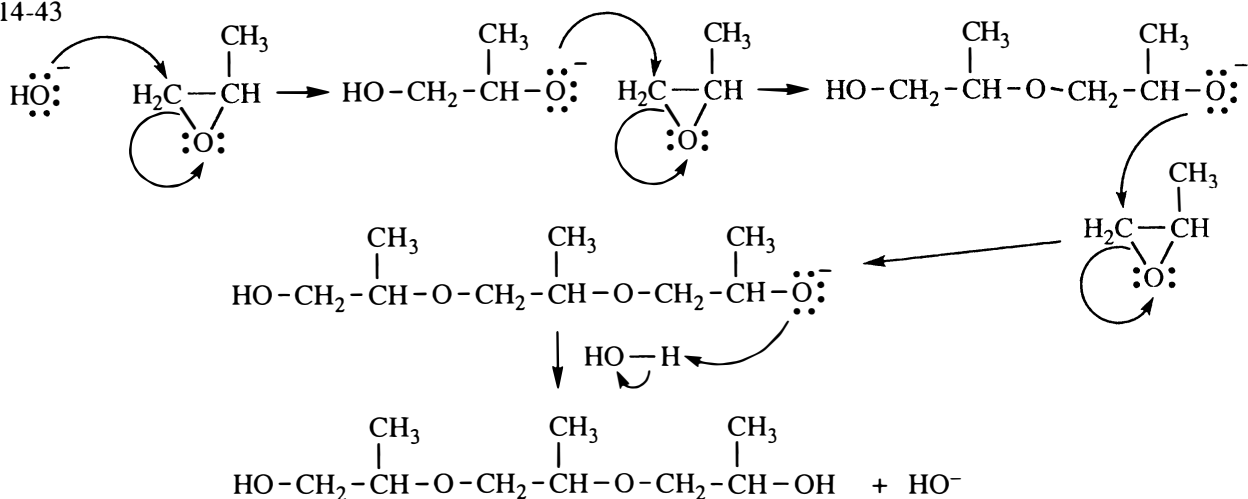


In the second reaction sequence, however, bonds to the chiral carbon are broken twice, so the stereochemistry of each process must be considered.

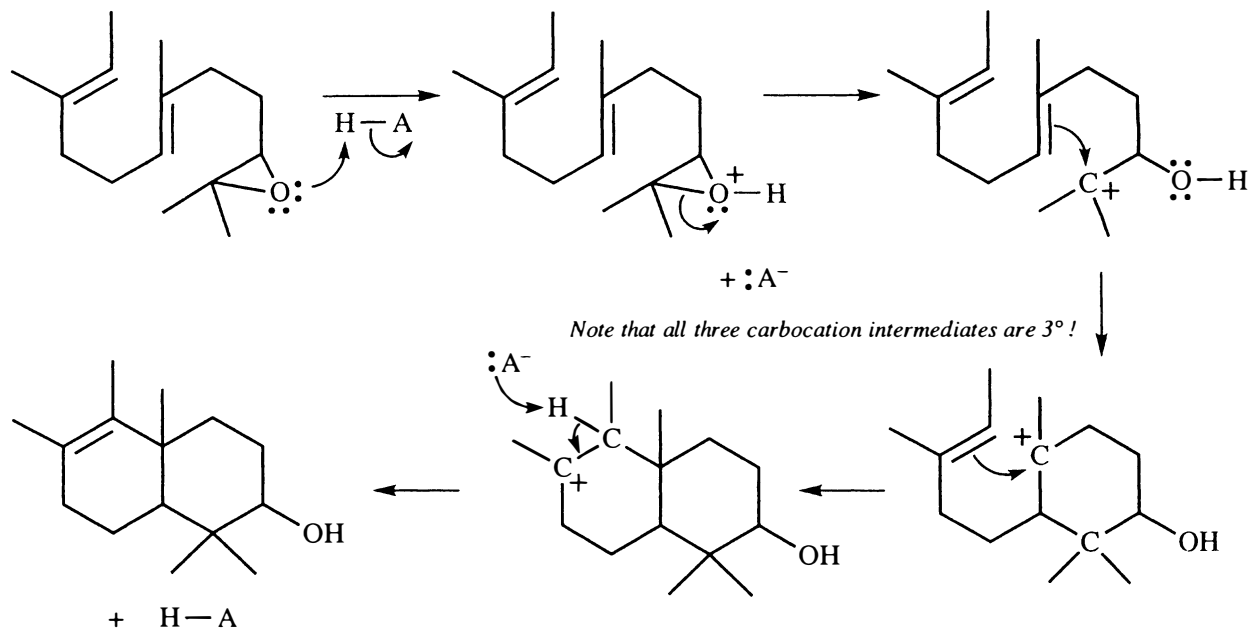


The second sequence involves *retention* followed by *inversion*, thereby producing the *enantiomer* of the 2-ethoxyoctane generated by the first sequence. The optical rotation of the final product will have equal magnitude but opposite sign, $[\alpha]_D = +15.6^\circ$.

14-43



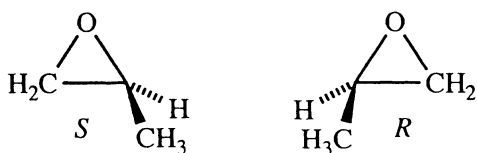
14-44 The text uses HA to indicate an acid; A^- is the conjugate base.



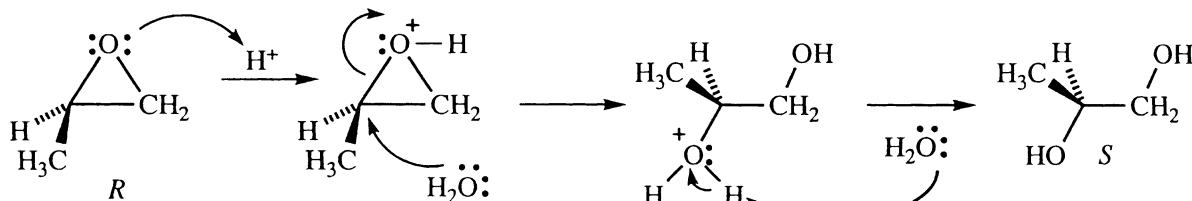
This process resembles the cyclization of squalene oxide to lanosterol. (See the solution to problem 14-24.) In fact, pharmaceutical synthesis of steroids uses the same type of reaction called a "biomimetic cyclization".

14-45

(a)

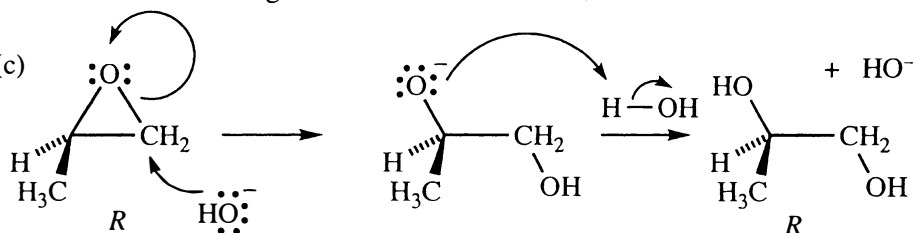


(b)



Attack of water gave *inversion* of configuration at the chiral center; *R* became *S*.

(c)



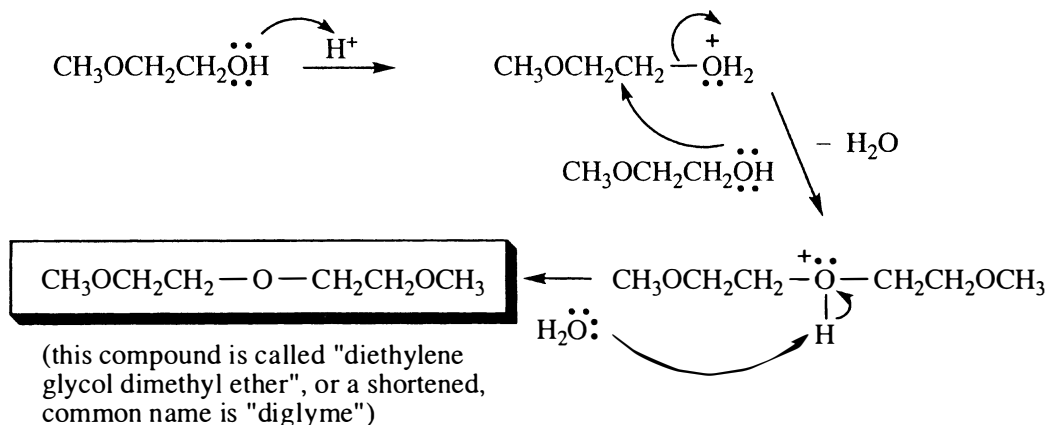
No bond to the chiral center was broken. Configuration is retained; *R* stays as *R*.

(d) The difference in these mechanisms lies in where the nucleophile attacks. Attack at the chiral carbon gives inversion; attack at the achiral carbon retains the configuration at the chiral carbon. These products are enantiomers and must necessarily have optical rotations of opposite sign.

14-46 methyl cellosolve $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OH}$

To begin, what can be said about methyl cellosolve? Its molecular weight is 76; its IR would show $\text{C}=\text{O}$ in the $1000\text{--}1200\text{ cm}^{-1}$ region and a strong $\text{O}=\text{H}$ around 3300 cm^{-1} ; and its NMR would show four sets of signals in the ratio of 3:2:2:1.

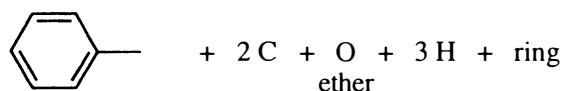
The unknown has molecular weight 134; this is double the weight of methyl cellosolve, minus 18 (water). The IR shows no OH, only ether $\text{C}=\text{O}$. The NMR shows no OH, only $\text{H}=\text{C}=\text{O}$ in the ratio of 3:2:2. Apparently, two molecules of methyl cellosolve have combined in an acid-catalyzed, bimolecular dehydration.



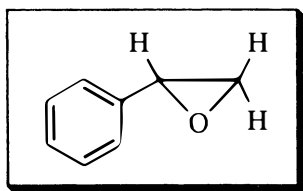
14-47

The formula C_8H_8O has five elements of unsaturation (enough (4) for a benzene ring). The IR is useful for what it does *not* show. There is neither OH nor $C=O$, so the oxygen must be an ether functional group.

The NMR shows a 5H signal at δ 7.2, a monosubstituted benzene. No peaks in the δ 4.5-6.0 range indicate the absence of an alkene, so the remaining element of unsaturation must be a ring. The three protons are non-equivalent, with complex splitting.

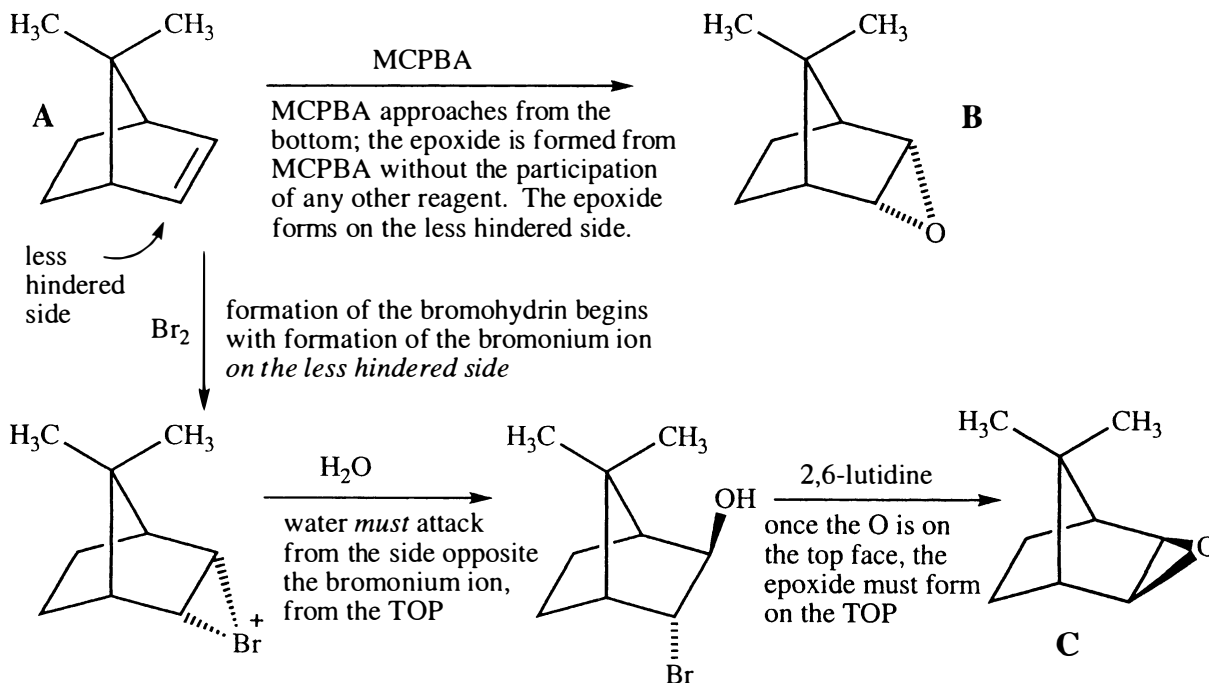


These pieces can be assembled in only one manner consistent with the data.



(Note that the CH_2 hydrogens are not equivalent (one is *cis* and one is *trans* to the phenyl) and therefore have distinct chemical shifts.)

14-48 The key concept is that reagents always go to the less hindered side of a molecule first. In this case, the "underneath" side is less hindered; the "top" side has a CH_3 hovering over the double bond and approach from the top will be much more difficult, and therefore slower, than approach from underneath.

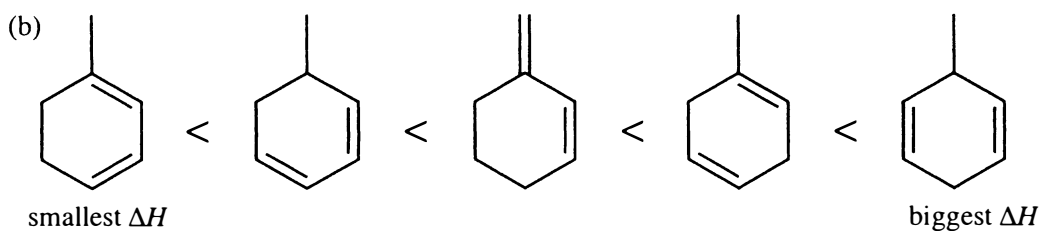
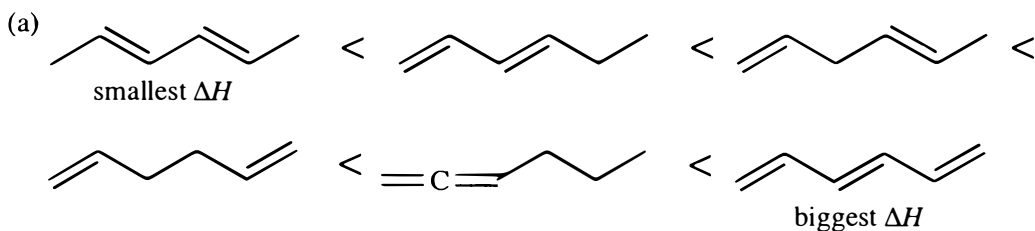


Epoxides **B** and **C** are diastereomers; they will have different chemical and physical properties. Nucleophiles can react with **C** much faster than with **B** for precisely the same reason that explained their formation: approach from underneath is less hindered and is faster than approach from the top.

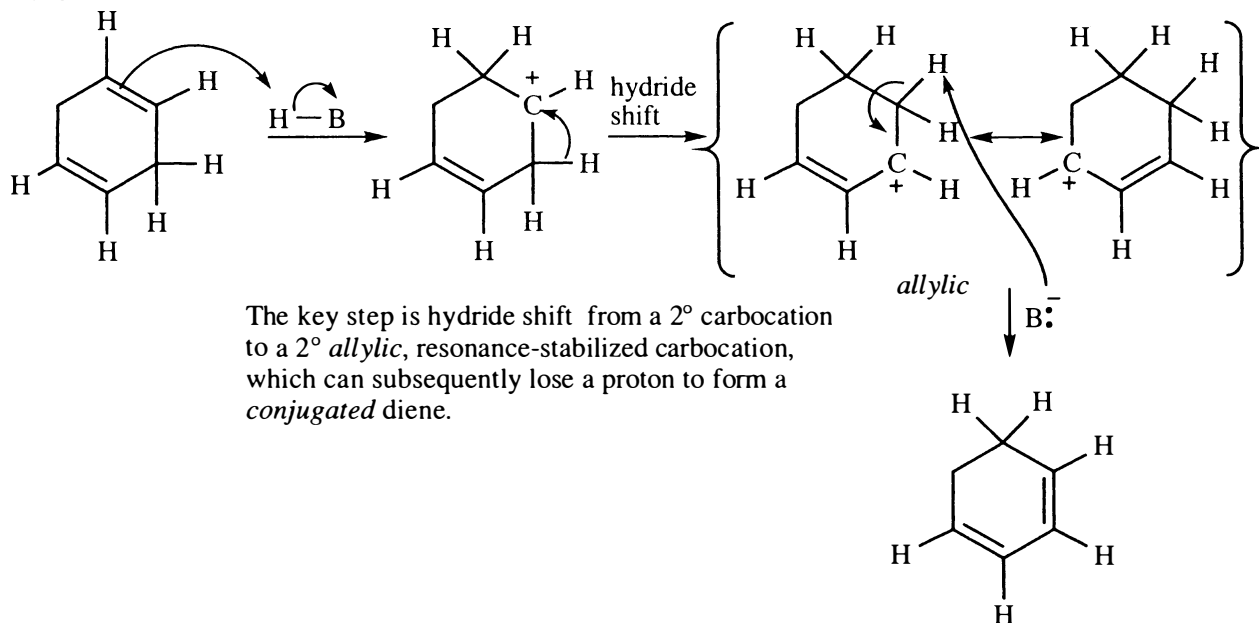
CHAPTER 15—CONJUGATED SYSTEMS, ORBITAL SYMMETRY, AND

ULTRAVIOLET SPECTROSCOPY

15-1 Look for: 1) the number of double bonds to be hydrogenated—the fewer C=C, the smaller the ΔH ; 2) conjugation—the more conjugated, the more stable, the lower the ΔH ; 3) degree of substitution of the alkenes—the more substituted, the more stable, the lower the ΔH .



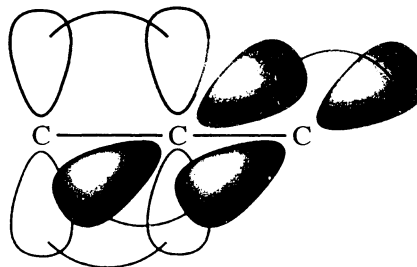
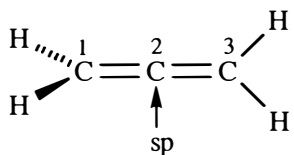
15-2 Reminder: $H-B$ is used to symbolize the general form for an acid, that is, a protonated base; B^- is the conjugate base.



15-3 (You may wish to refer to problem 2-6.)

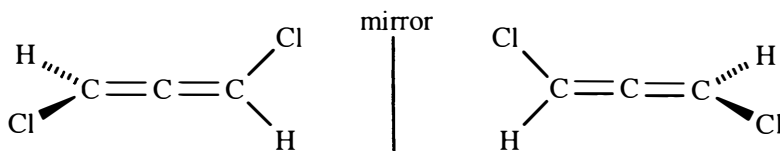
orbital picture

(a)



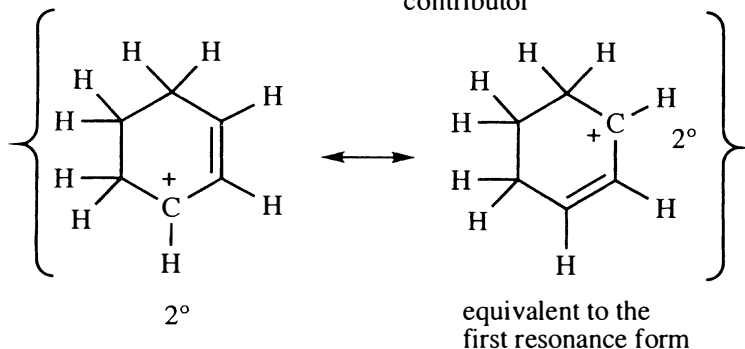
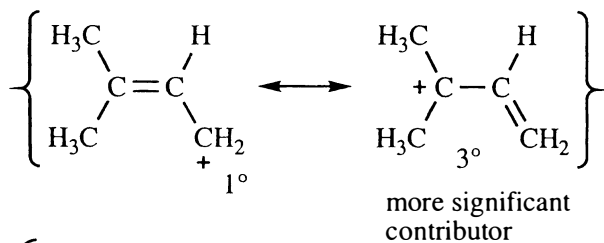
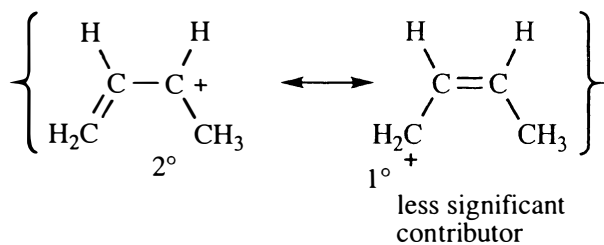
The central carbon atom makes two π bonds with two p orbitals. These p orbitals must necessarily be perpendicular to each other, thereby forcing the groups on the ends of the allene system perpendicular.

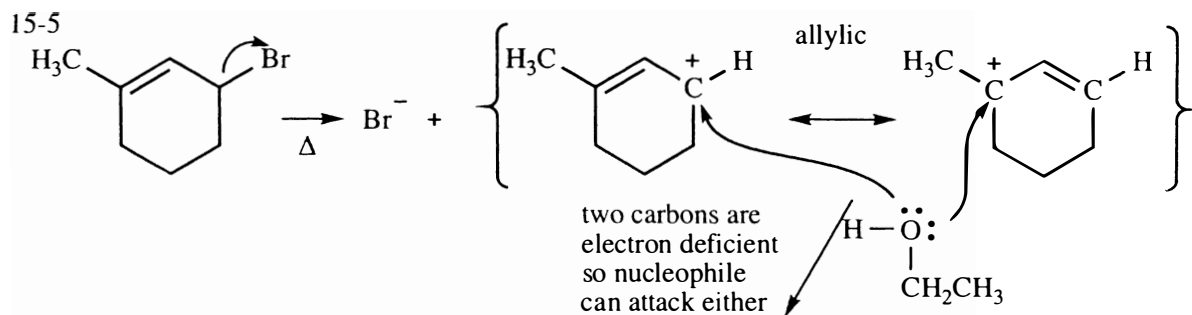
(b)



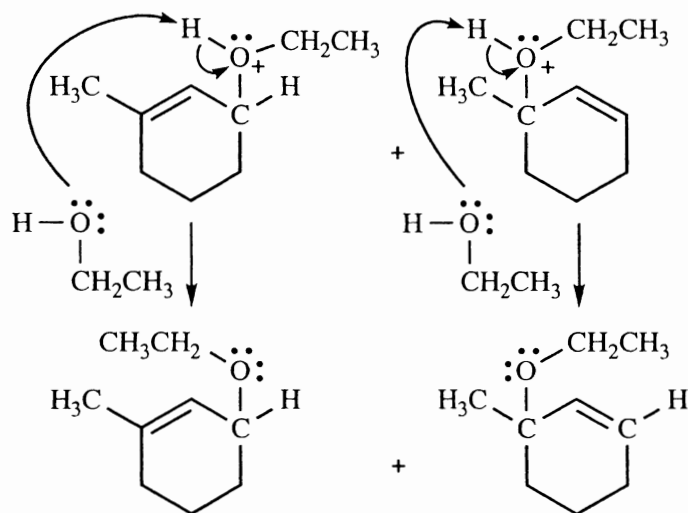
non-superimposable mirror images = enantiomers

15-4 Carbocation stability depends on conjugation (benzylic, allylic), then on degree of carbon carrying the positive charge.

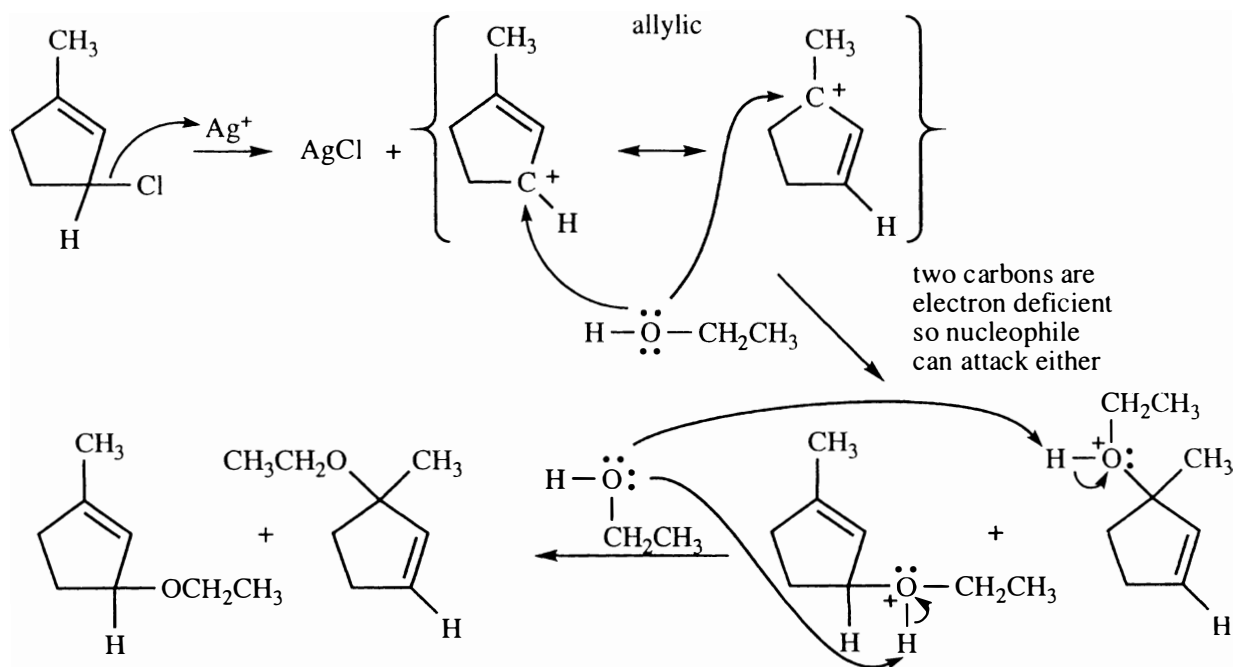




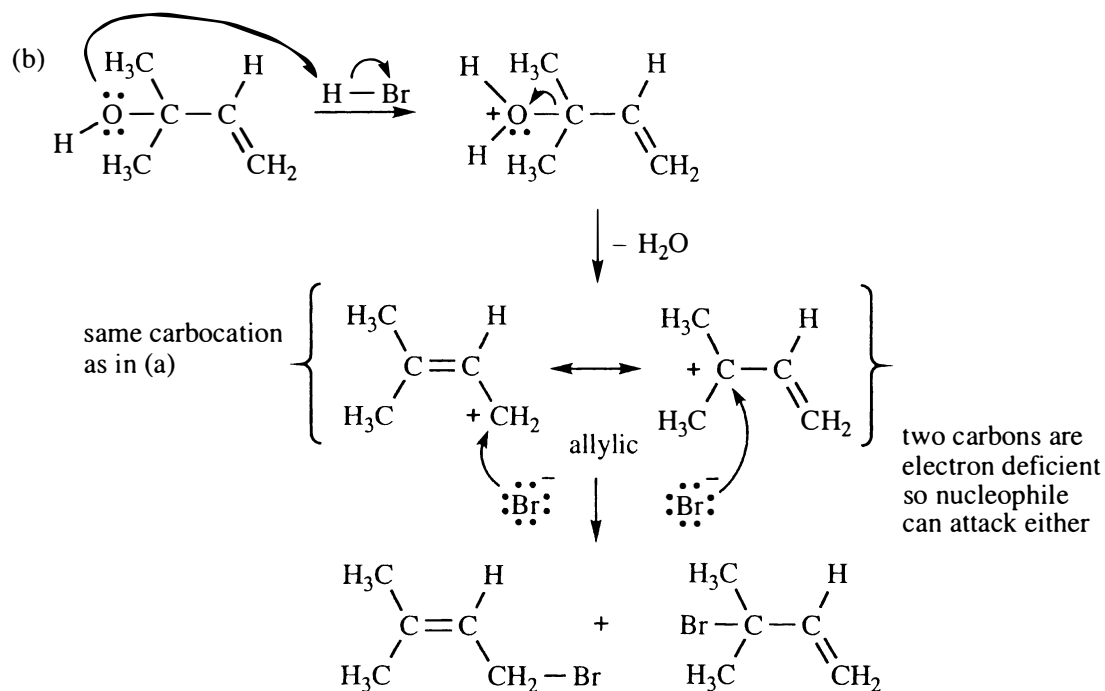
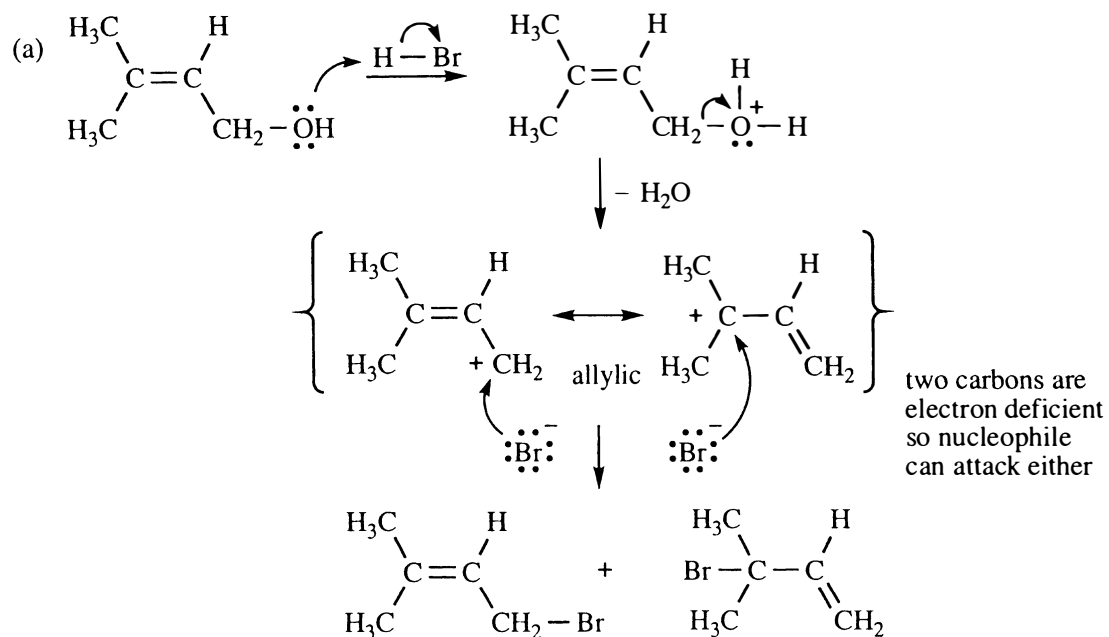
The most basic species in the reaction mixture will remove this proton. The oxygen of ethanol is more basic than bromide ion.



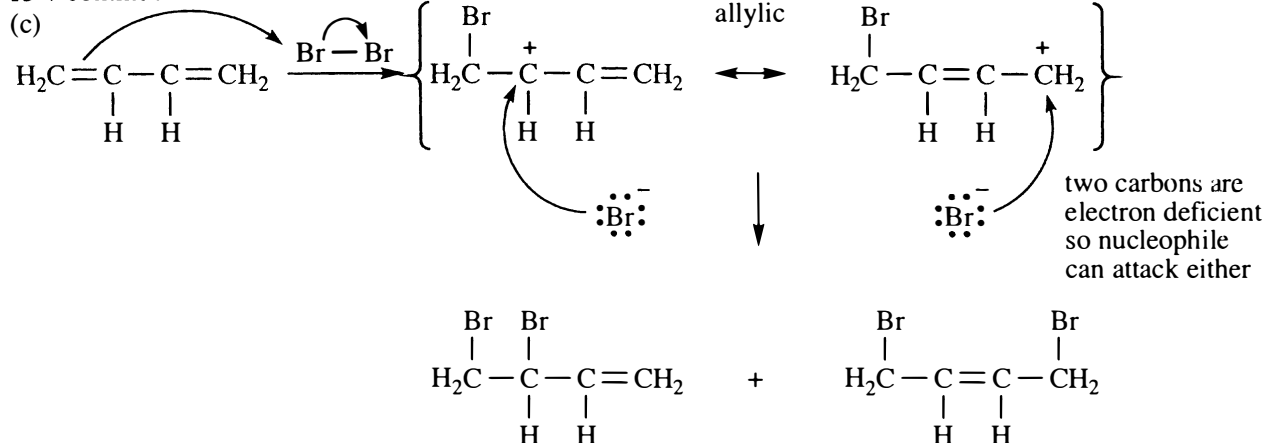
15-6



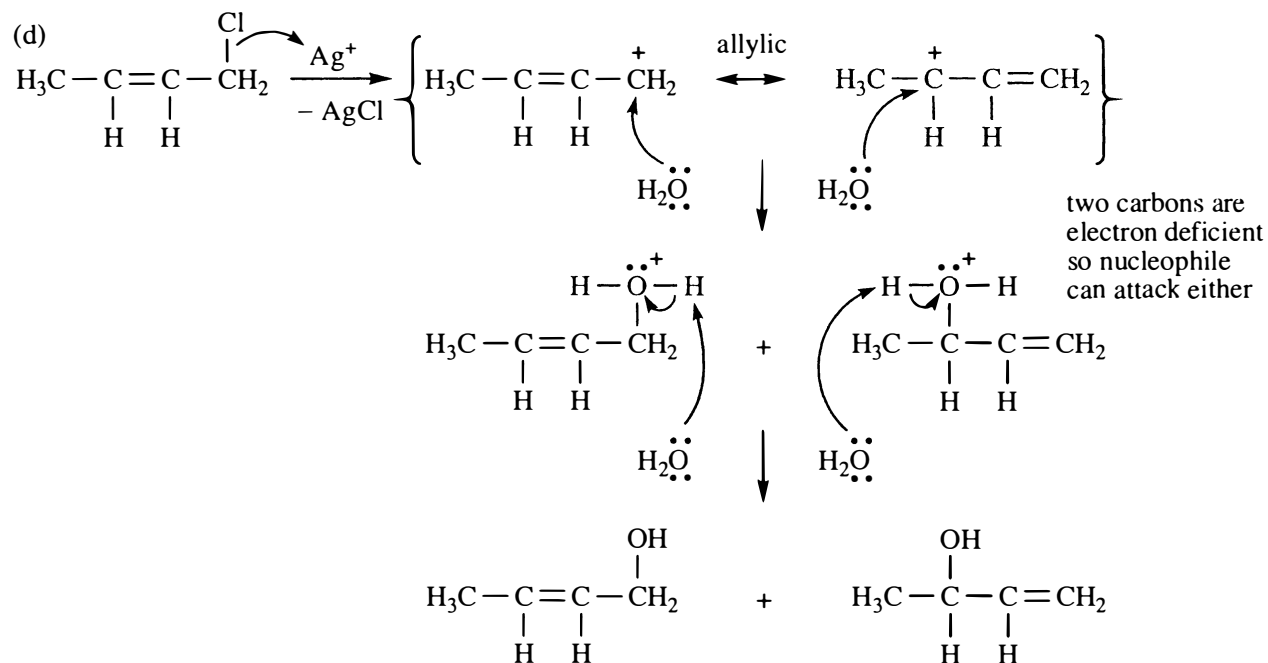
15-7



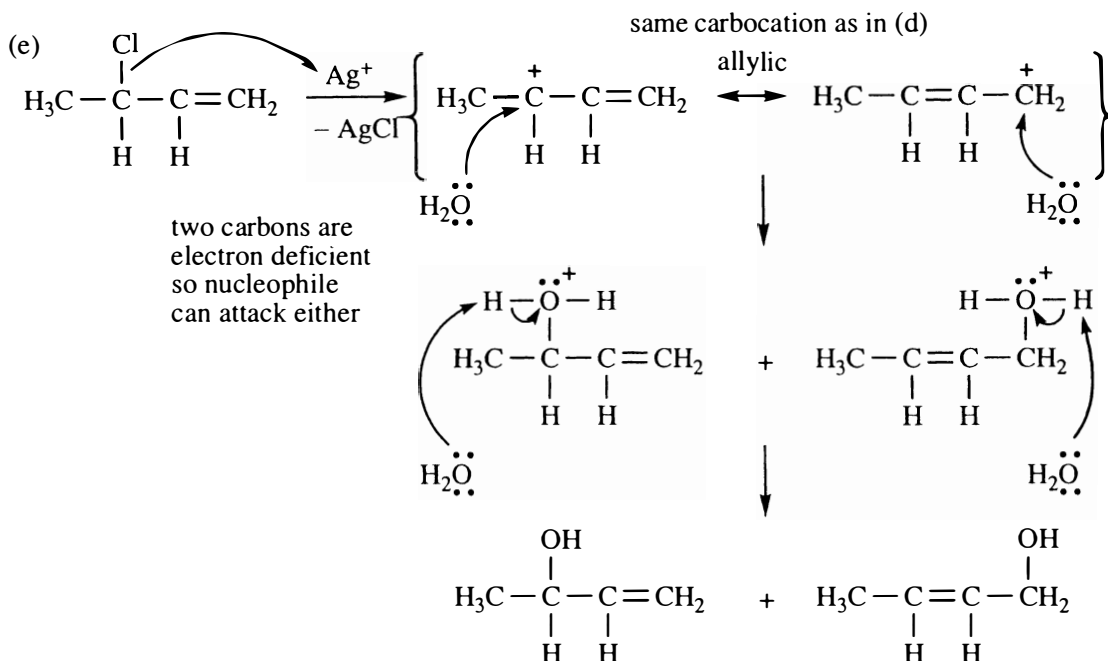
15-7 continued



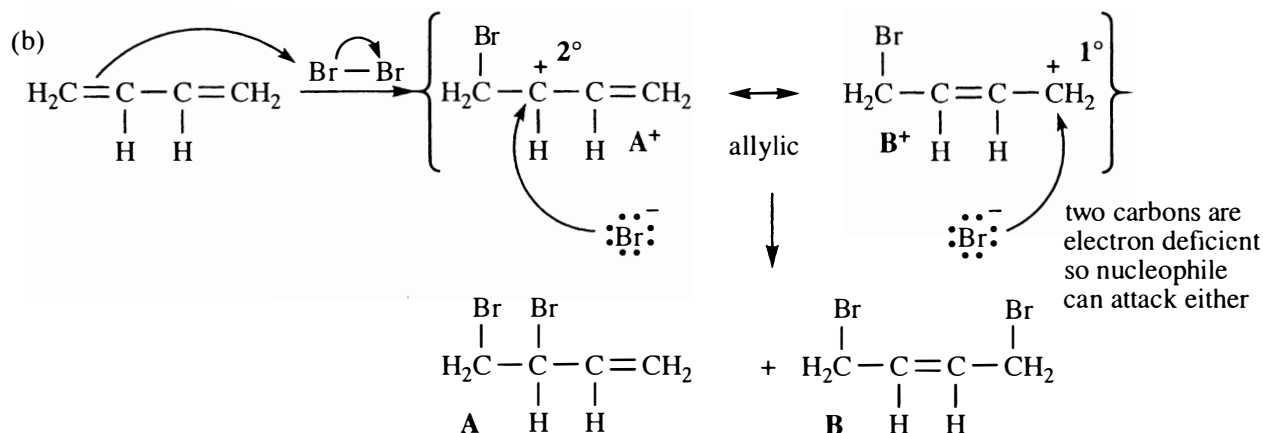
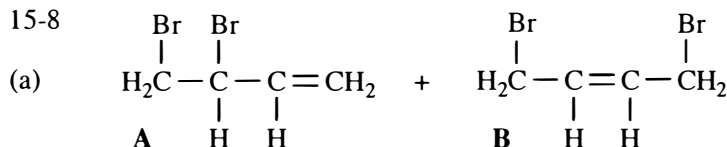
While the bromonium ion mechanism is typical for isolated alkenes, the greater stability of the resonance-stabilized carbocation will make it the lower energy intermediate for conjugated systems.



15-7 continued



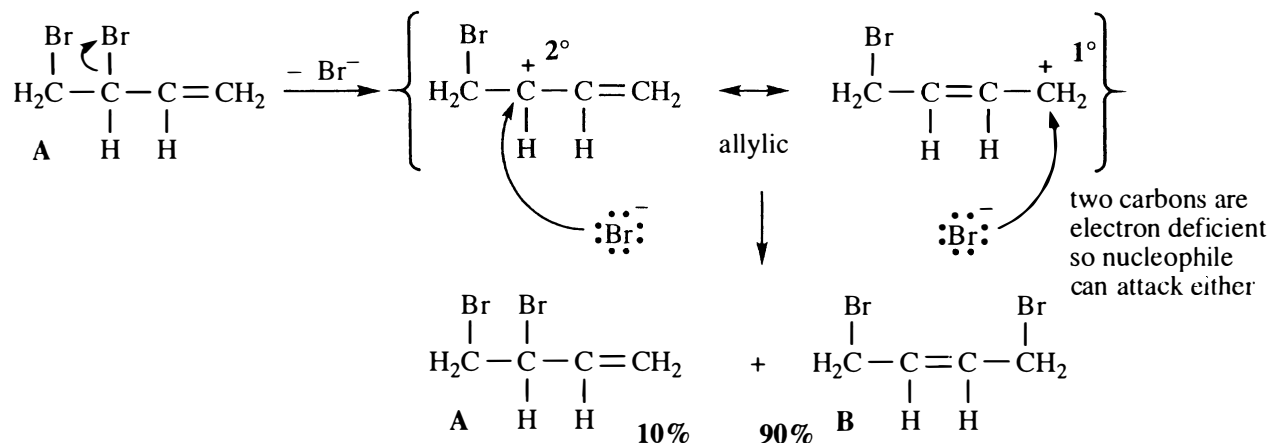
15-8



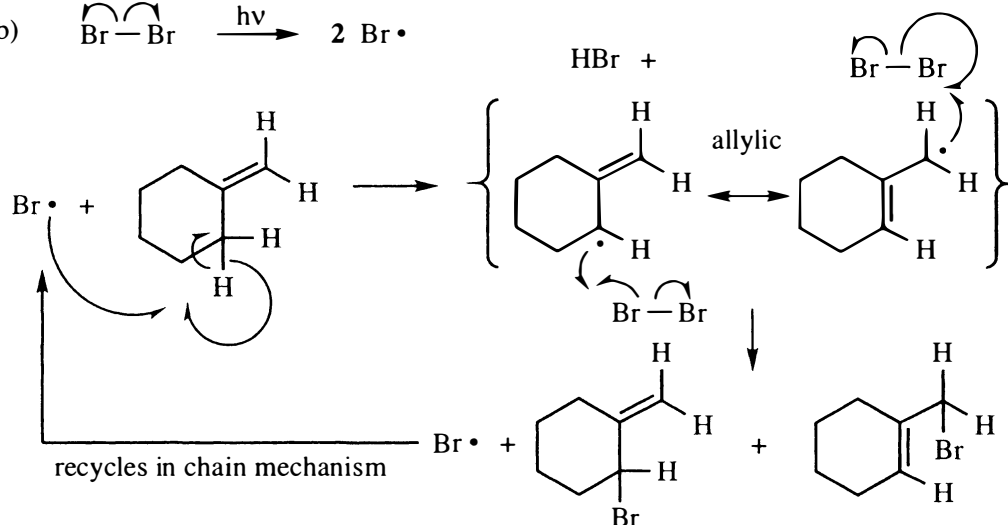
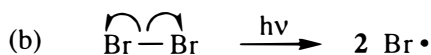
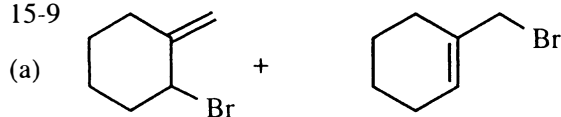
(c) The resonance form A^+ , which eventually leads to product **A**, has positive charge on a 2° carbon and is a more significant resonance contributor than structure B^+ . With greater positive charge on the 2° carbon than on the 1° carbon, we would expect bromide ion attack on the 2° carbon to have lower activation energy. Therefore, **A** must be the *kinetic* product. At higher temperature, however, the last step becomes reversible, and the stability of the products becomes the dominant factor in determining product ratios. As **B** has a disubstituted alkene whereas **A** is only monosubstituted, it is reasonable that **B** is the major, *thermodynamic* product at 60°C .

15-8 continued

(d) At 60° C, ionization of **A** would lead to the same allylic carbocation as shown in (b), which would give the same product ratio as formation of **A** and **B** from butadiene.

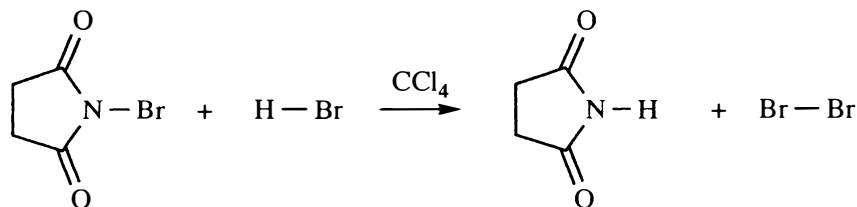


15-9

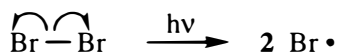
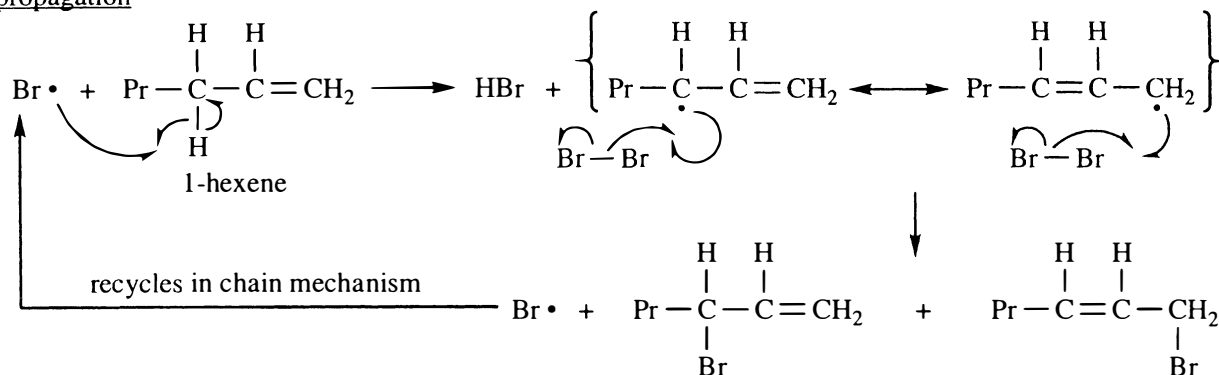


15-10 ("Pr" is the abbreviation for *n*-propyl, used below.)

NBS generates a low concentration of Br_2

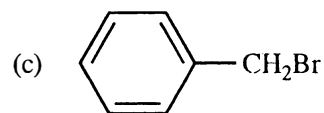
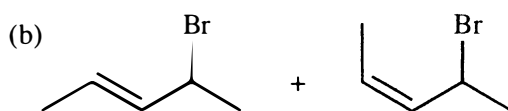
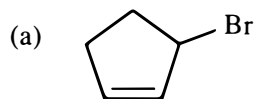


15-10 continued

initiationpropagation

The HBr generated in the propagation step combines with NBS to produce more Br_2 , continuing the chain mechanism.

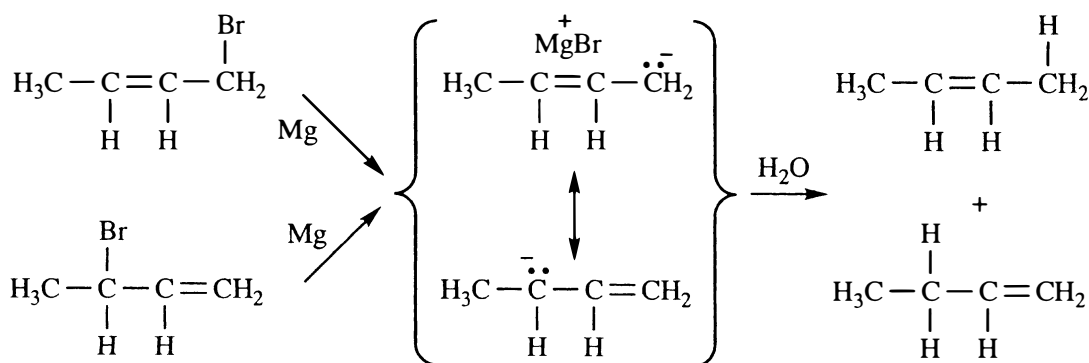
15-11



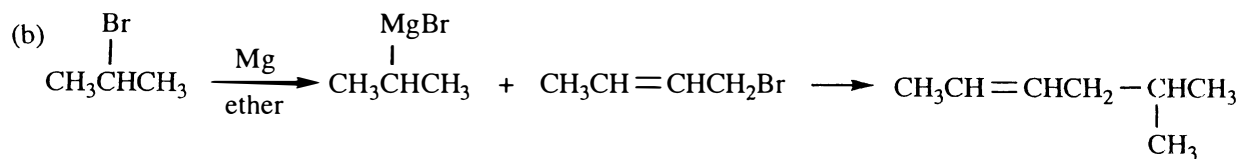
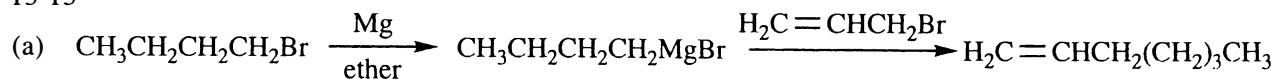
These are the major products from abstraction of a 2° allylic H.

benzylic radicals are even more stable than allylic

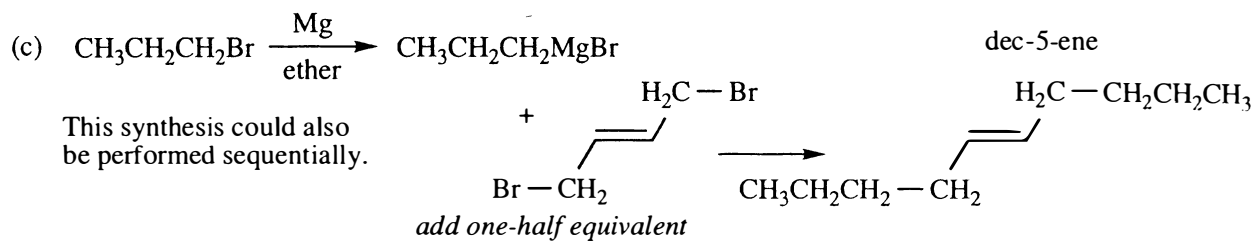
15-12 Both halides generate the same allylic carbanion.



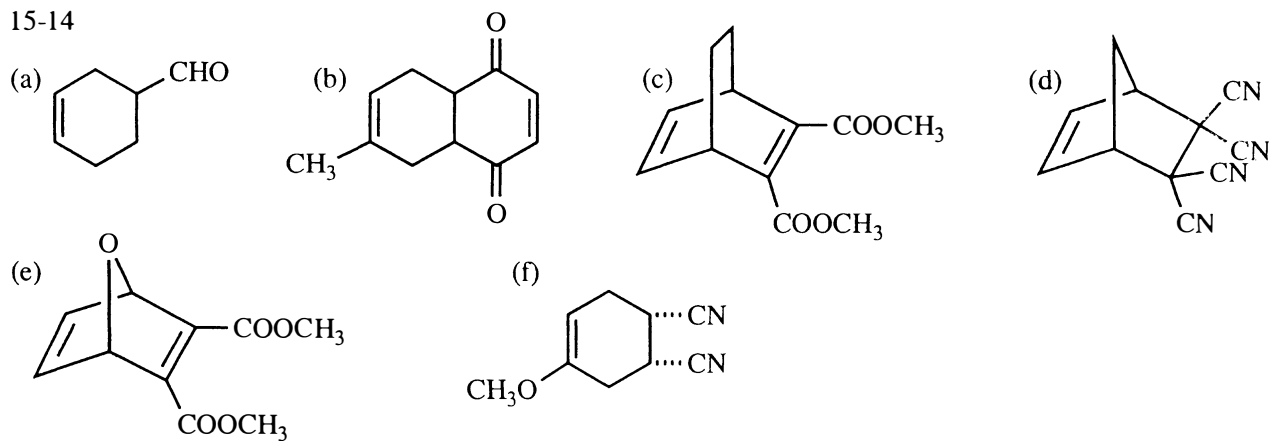
15-13



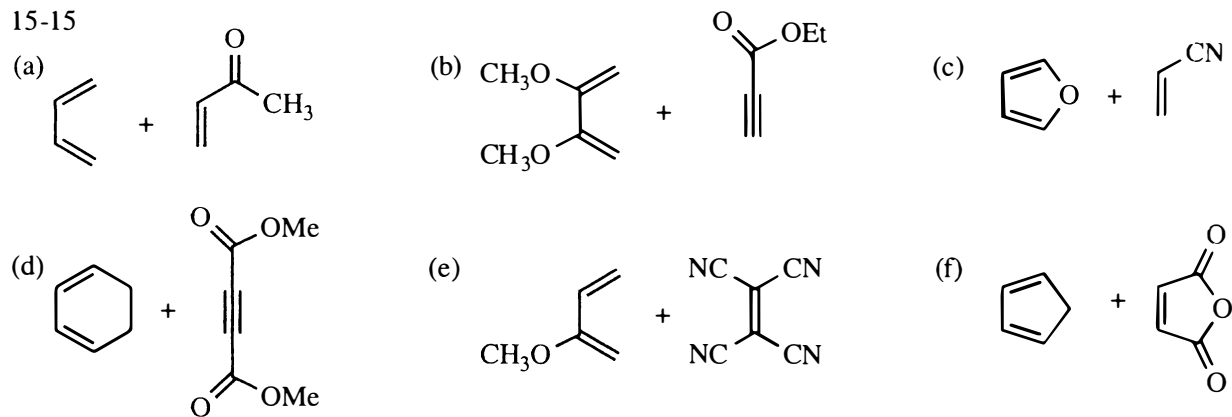
15-13 continued



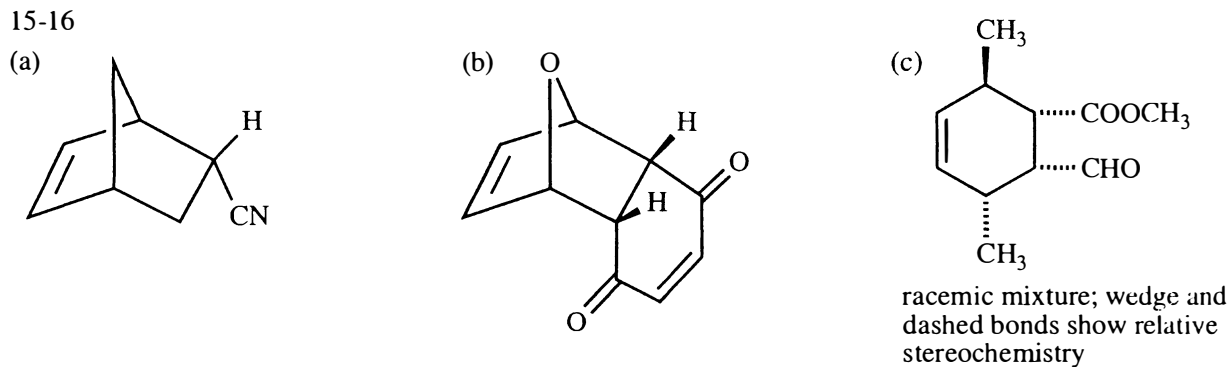
15-14



15-15

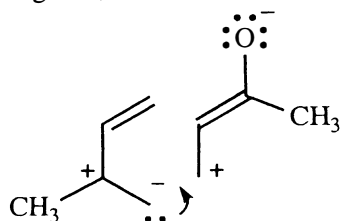


15-16



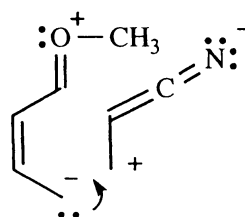
15-17 These structures show the alignment of diene and dienophile in the Diels-Alder transition state, leading to 1,4-orientation in (a) and 1,2-orientation in (b).

(a)



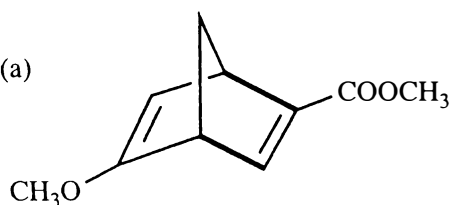
this left structure is a VERY minor resonance contributor; however, it explains the orientation for the diene as carbon-1 is more negative and carbon-2, a 3° C, is slightly more positive because of methyl group stabilization

(b)

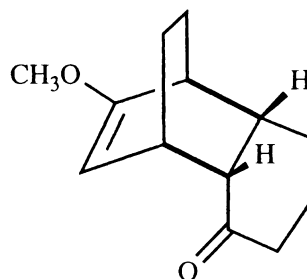


15-18 For clarity, the bonds formed in the Diels-Alder reaction are shown in bold.

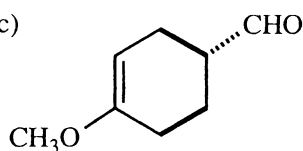
(a)



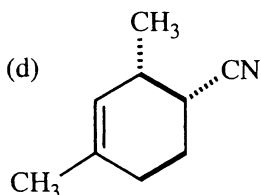
(b)



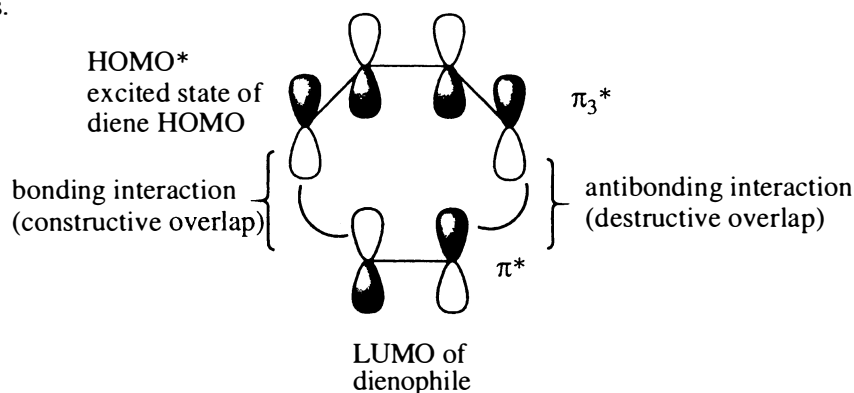
(c)



(d)



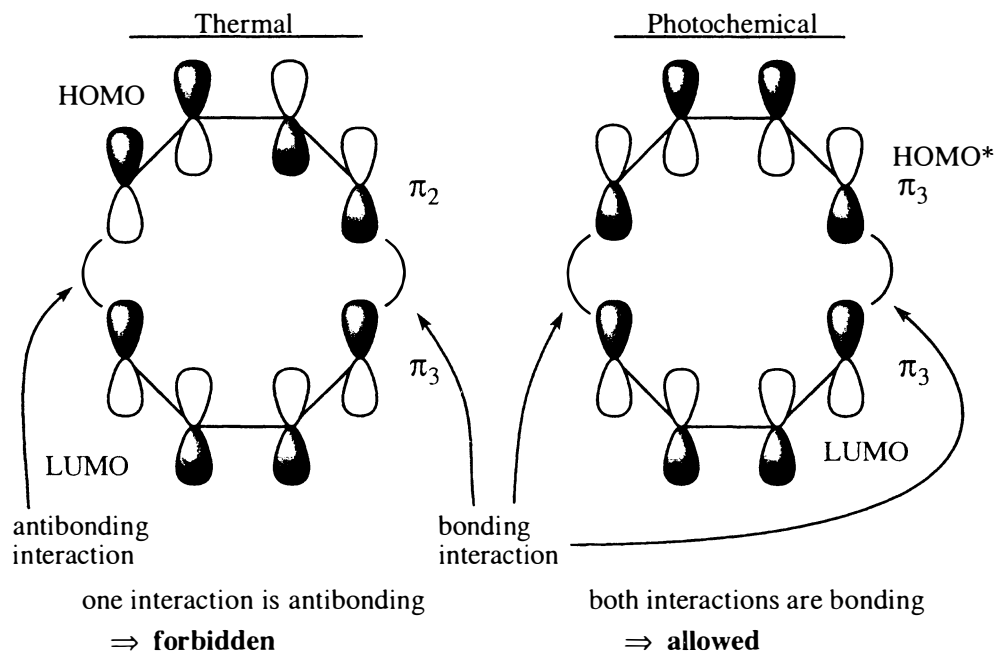
15-19 For a photochemically *allowed* process, one molecule must use an excited state in which an electron has been promoted to the first antibonding orbital. All orbital interactions between the excited molecule's HOMO* and the other molecule's LUMO must be bonding for the interaction to be allowed; otherwise, it is a forbidden process.



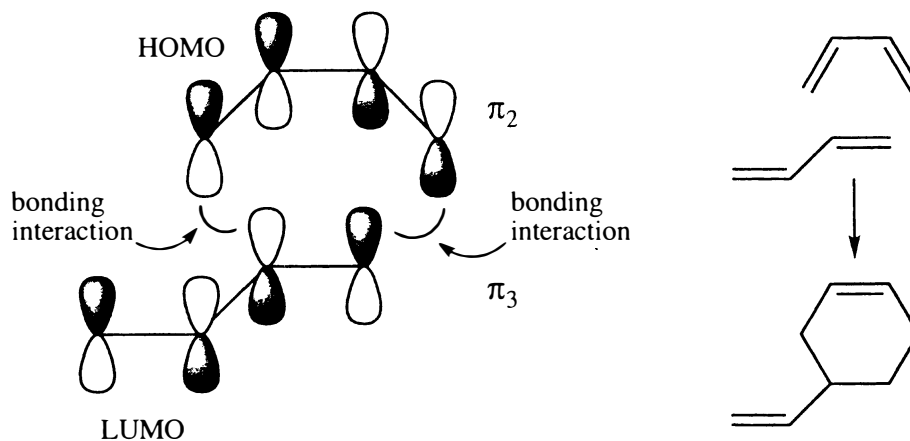
In the Diels-Alder cycloaddition, the LUMO of the dienophile and the excited state of the HOMO of the diene (labeled HOMO*) produce one bonding interaction and one antibonding interaction. Thus, this is a photochemically forbidden process.

15-20 For a [4 + 4] cycloaddition:

(a)



(b) A [4 + 4] cycloaddition is not thermally allowed, but a [4 + 2] (Diels-Alder) is!



15-21

$$A = \epsilon c l \quad \epsilon = \frac{A}{c l} \quad l = 1 \text{ cm} \quad A = 0.50$$

convert mass to moles: $1 \text{ mg} \times \frac{1 \text{ g}}{1000 \text{ mg}} \times \frac{1 \text{ mole}}{160 \text{ g}} = 6 \times 10^{-6} \text{ moles}$

$$c = \frac{6 \times 10^{-6} \text{ moles}}{10 \text{ mL}} \times \frac{1000 \text{ mL}}{1 \text{ L}} = 6 \times 10^{-4} \text{ M}$$

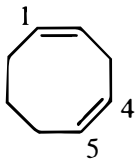
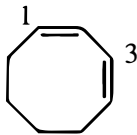
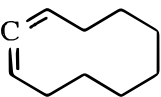
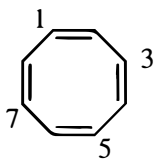
$$\epsilon = \frac{0.50}{(6 \times 10^{-4})(1)} = 833 \approx \boxed{800}$$

15-22

- (a) 353 nm: a conjugated tetraene—must have highest absorption maximum among these compounds;
 (b) 313 nm: closest to the bicyclic conjugated triene in Table 15-2; the diene is in a more substituted ring, so it is not surprising for the maximum to be slightly higher than 304 nm;
 (c) 232 nm: similar to 3-methylenecyclohexene in Table 15-2;
 (d) 273 nm: 1,3 cyclohexadiene (256 nm) + 2 alkyl substituents (2 x 5 nm) = predicted value of 266 nm;
 (e) 237 nm: like 3-methylenecyclohexene (232 nm) + 1 alkyl group (5 nm) = predicted value of 237 nm

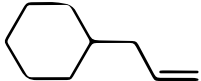
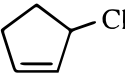
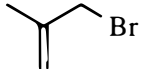
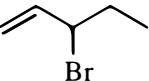
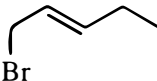
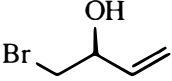
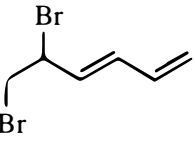
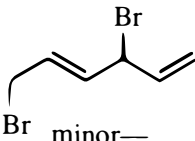
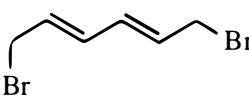
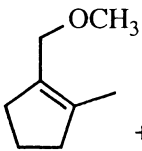
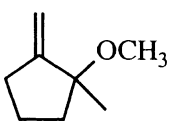
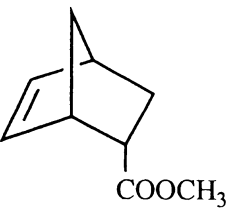
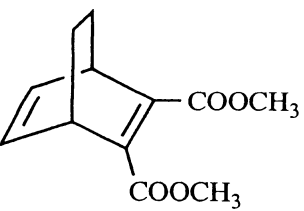
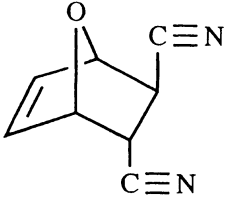
15-23 Please refer to solution 1-20, page 12 of this Solutions Manual.

15-24

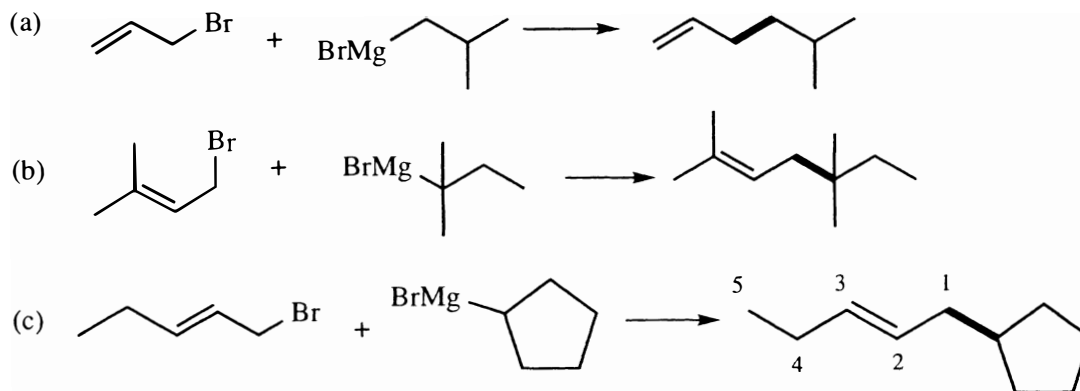
- (a) isolated  (b) conjugated  (c) cumulated  (d) conjugated  (e) conjugated 
 (f) cumulated (1,2) and conjugated (2,4)

$$\text{H}_2\text{C}=\text{C}=\underset{\text{H}}{\text{C}}-\underset{\text{H}}{\text{C}}=\text{CH}_2$$

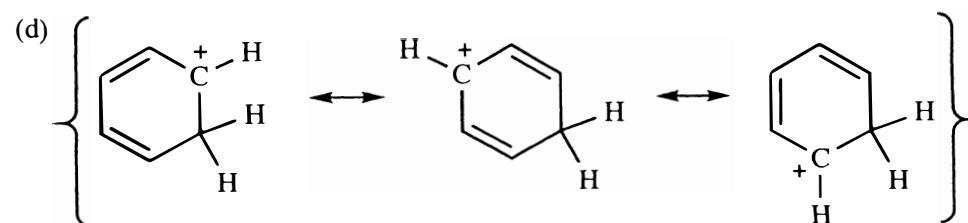
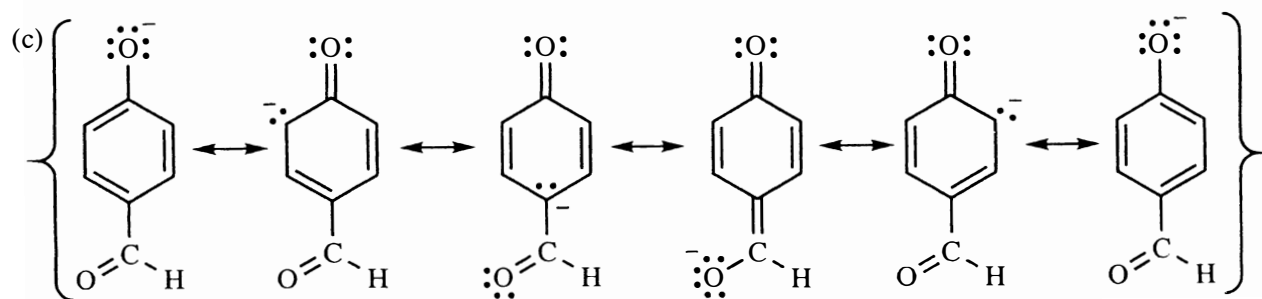
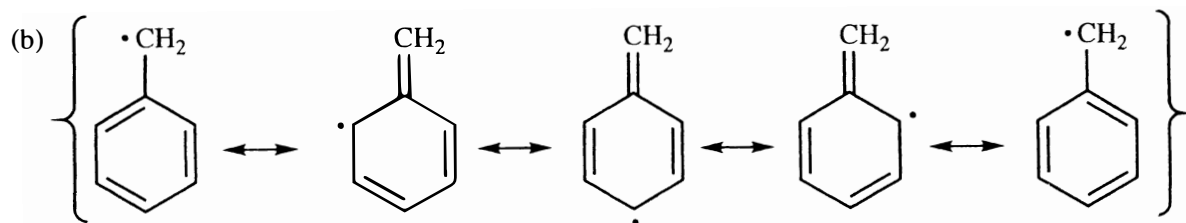
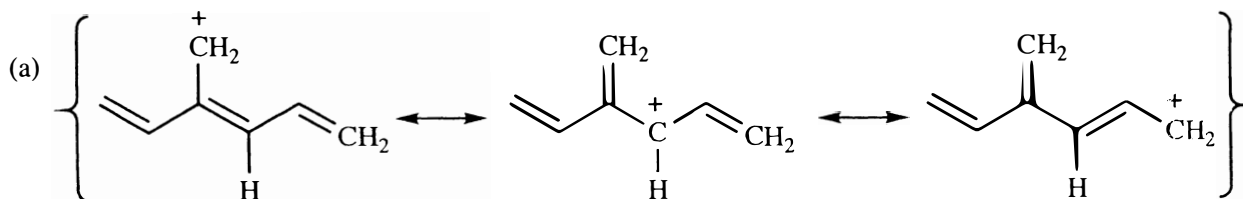
15-25

- (a)  (b)  one equivalent of HCl
 (c) 
 (d)  + 
 (e)  + 
 (f)  +  minor—not conjugated + 
 (g)  + 
 (h) 
 (i) 
 (j) 

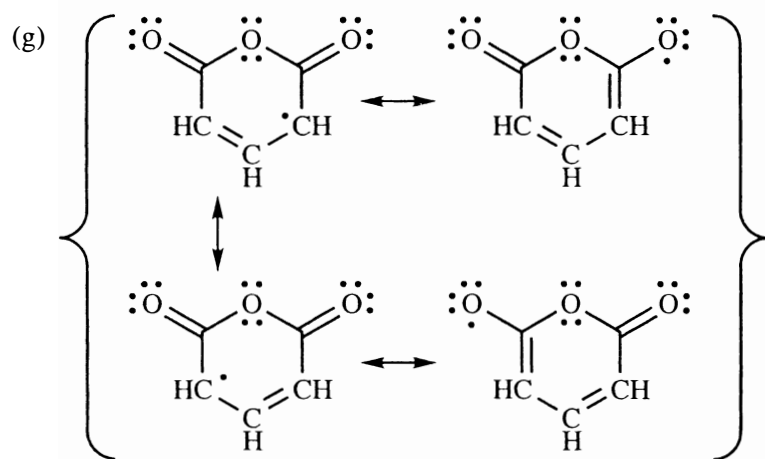
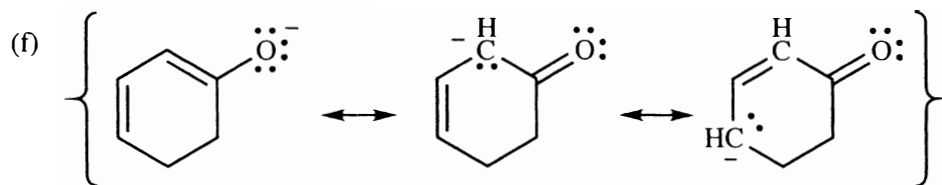
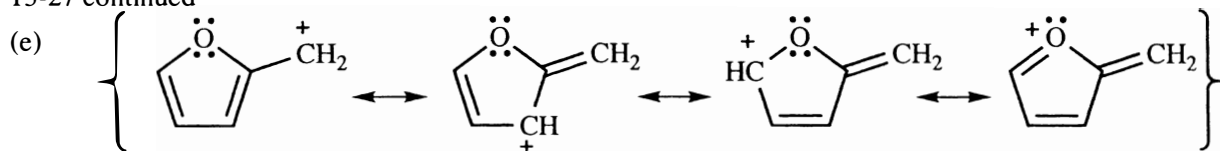
15-26 Grignard reactions are performed in ether solvent. For clarity, the bonds formed are shown in bold.



15-27



15-27 continued



15-28

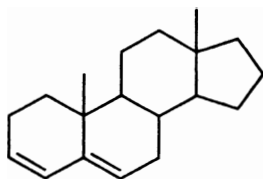
(a) $A = \epsilon c l$ $\epsilon = \frac{A}{c l}$ $l = 1 \text{ cm}$ $A = 0.74$

convert mass to moles: $0.0010 \text{ g} \times \frac{1 \text{ mole}}{255 \text{ g}} = 3.9 \times 10^{-6} \text{ moles}$

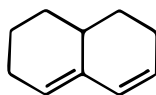
$c = \frac{3.9 \times 10^{-6} \text{ moles}}{100 \text{ mL}} \times \frac{1000 \text{ mL}}{1 \text{ L}} = 3.9 \times 10^{-5} \text{ M}$

$\epsilon = \frac{0.74}{(3.9 \times 10^{-5})(1)} \approx \boxed{19,000}$

(b) This large value of ϵ could only come from a conjugated system, eliminating the first structure. The absorption maximum at 235 nm is most likely a diene rather than a triene. The most reasonable structure is:

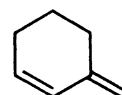


compare with:



$\lambda_{\text{max}} = 235 \text{ nm}$

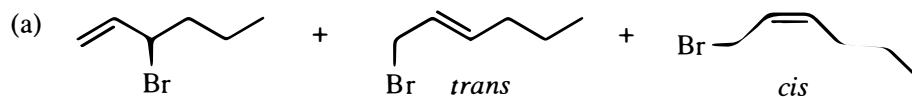
Solved Problem 15-3



$\lambda_{\text{max}} = 232 \text{ nm}$

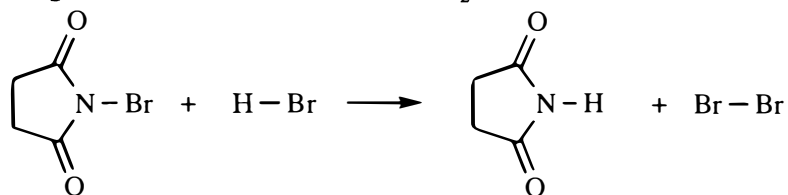
Table 15-2

15-29

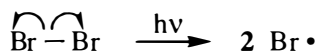


(b) ("Pr" is the abbreviation for *n*-propyl, used below.)

NBS generates a low concentration of Br₂

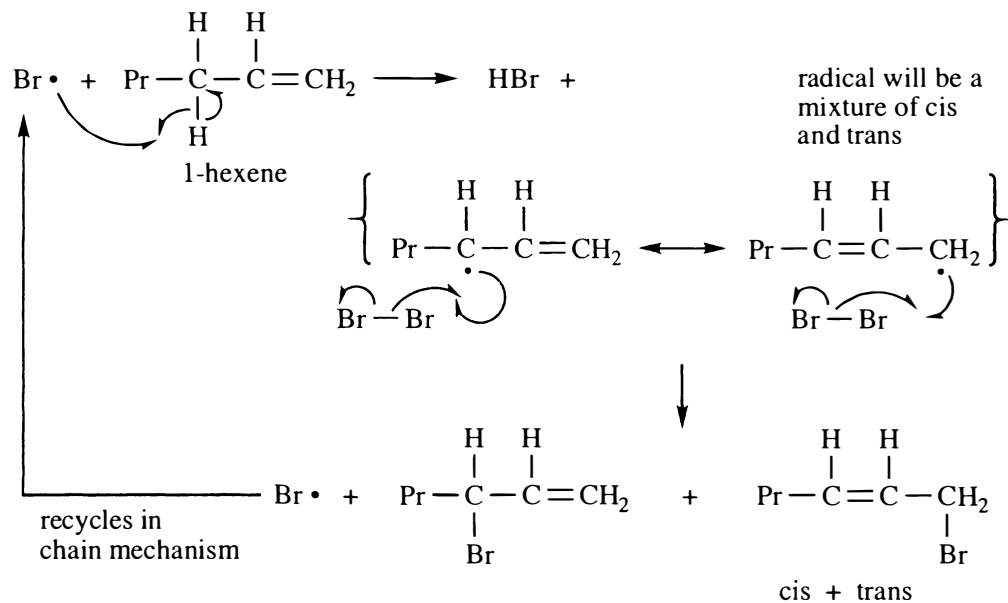


initiation

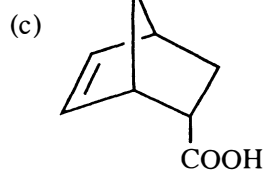
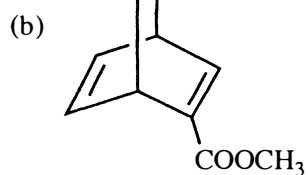
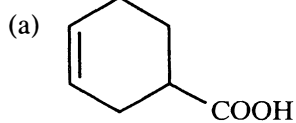


propagation

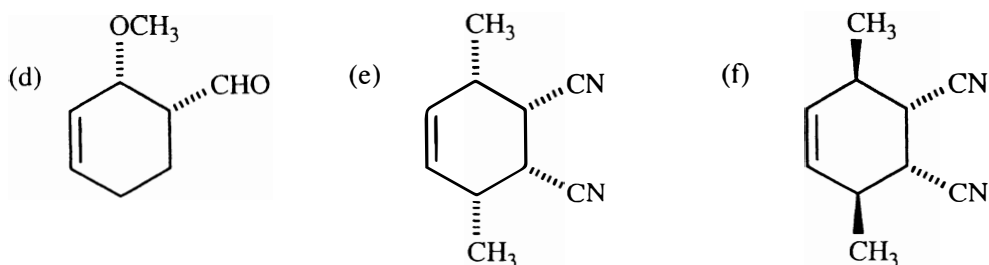
first step is abstraction of allylic hydrogen to generate allylic radical



15-30

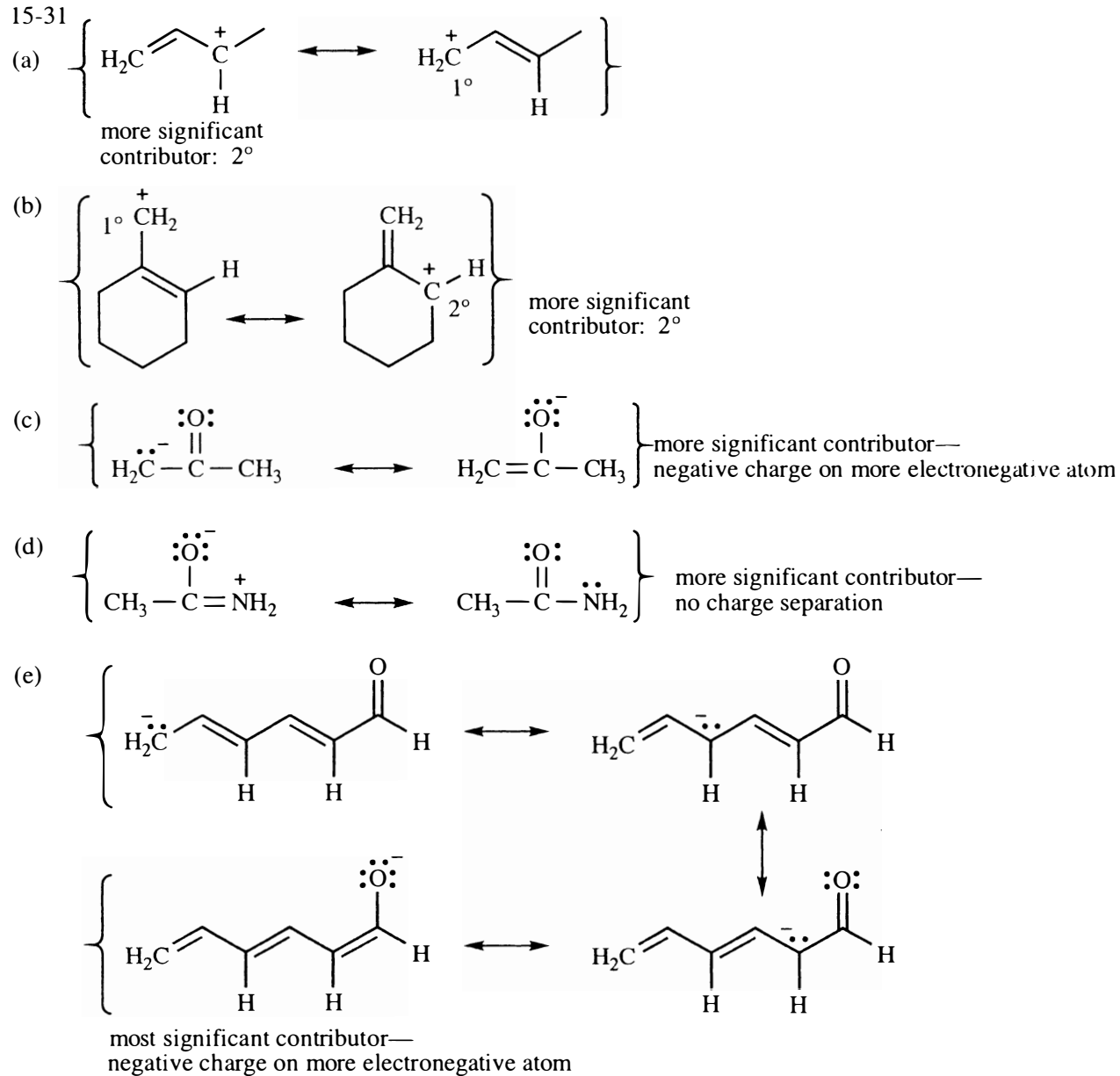


15-30 continued

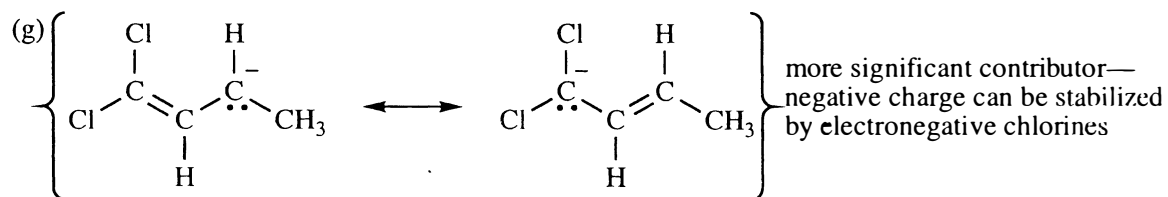
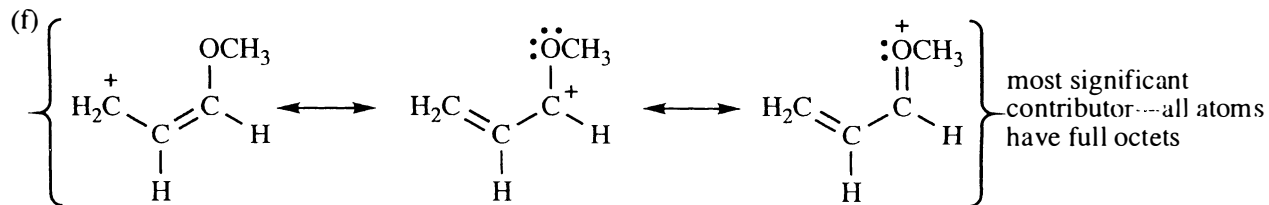


(Note: Yield of the product in (f) would be small or zero due to severe steric interaction in the *s-cis* conformation of the diene. See Figure 15-16.)

15-31

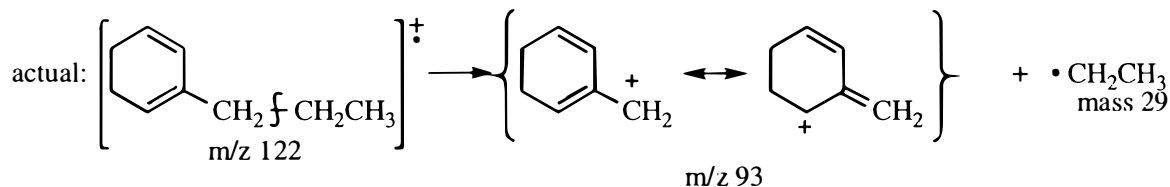
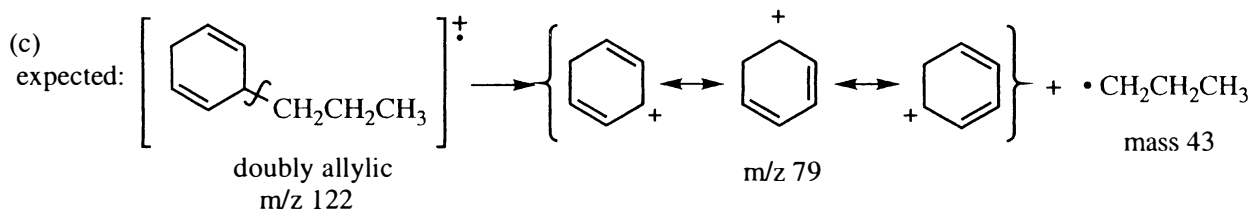
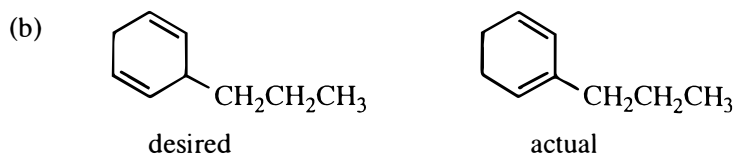


15-31 continued

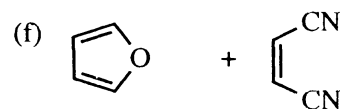
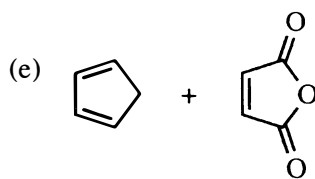
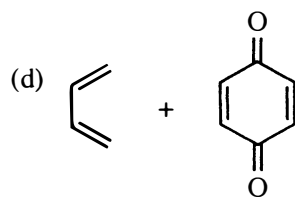
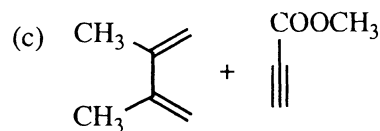
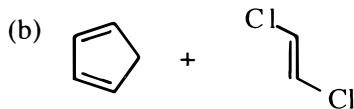
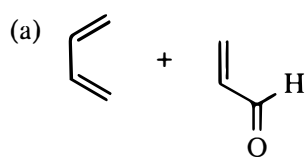


15-32

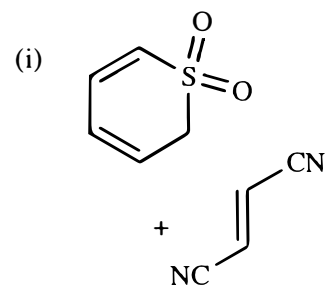
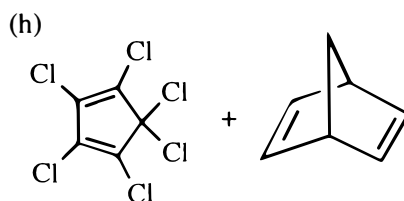
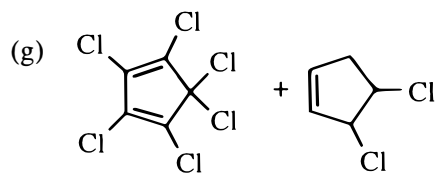
(a) The absorption at 1630 cm^{-1} suggests a conjugated alkene. The higher temperature allowed for migration of the double bond.



15-33

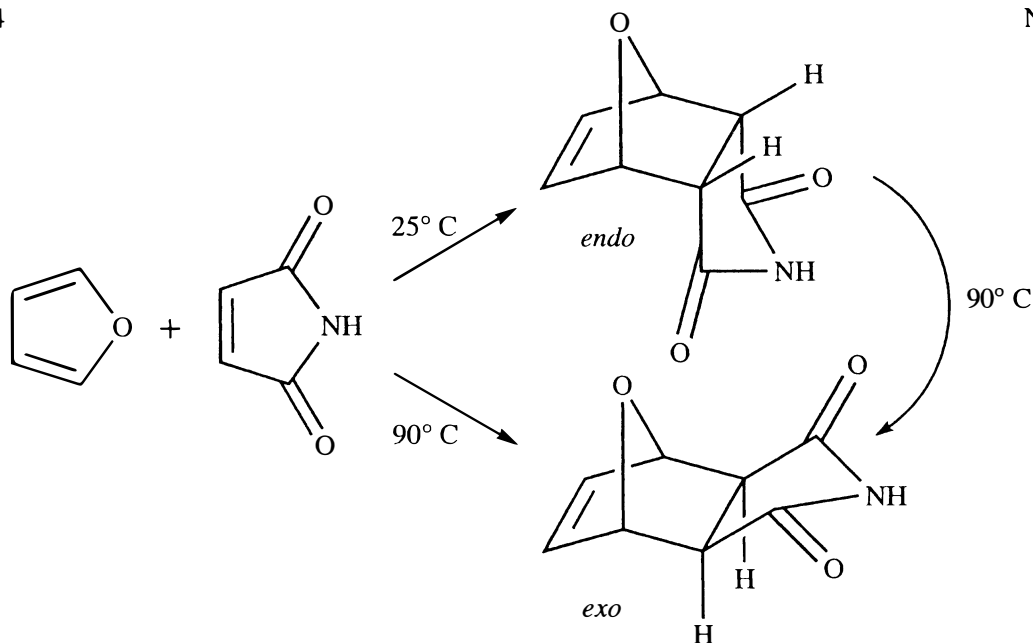


15-33 continued



15-34

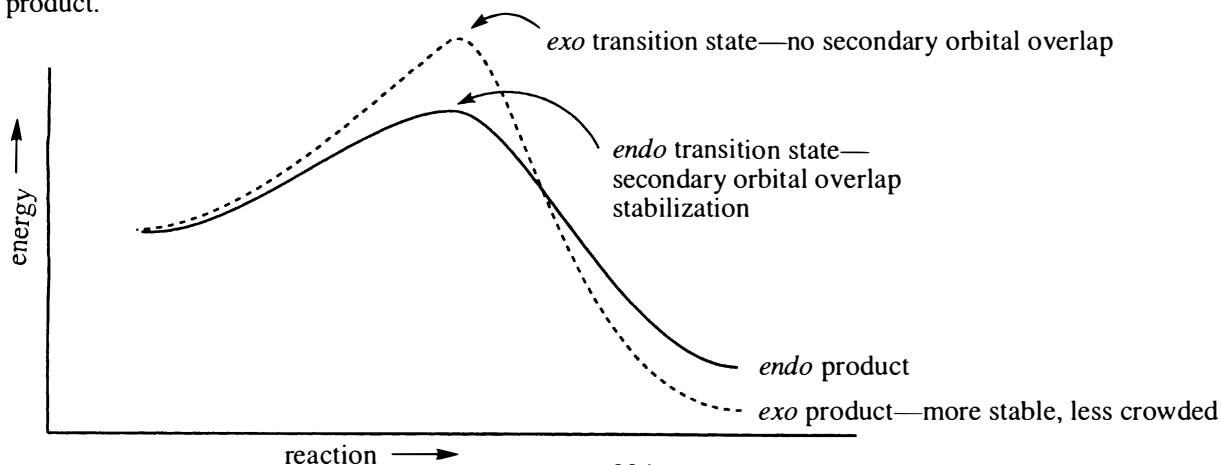
(a)



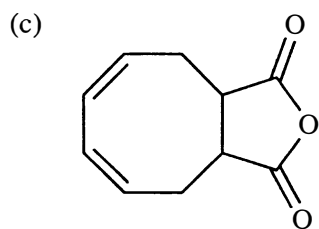
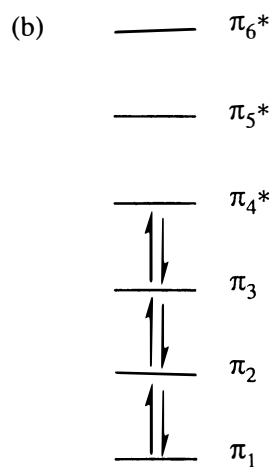
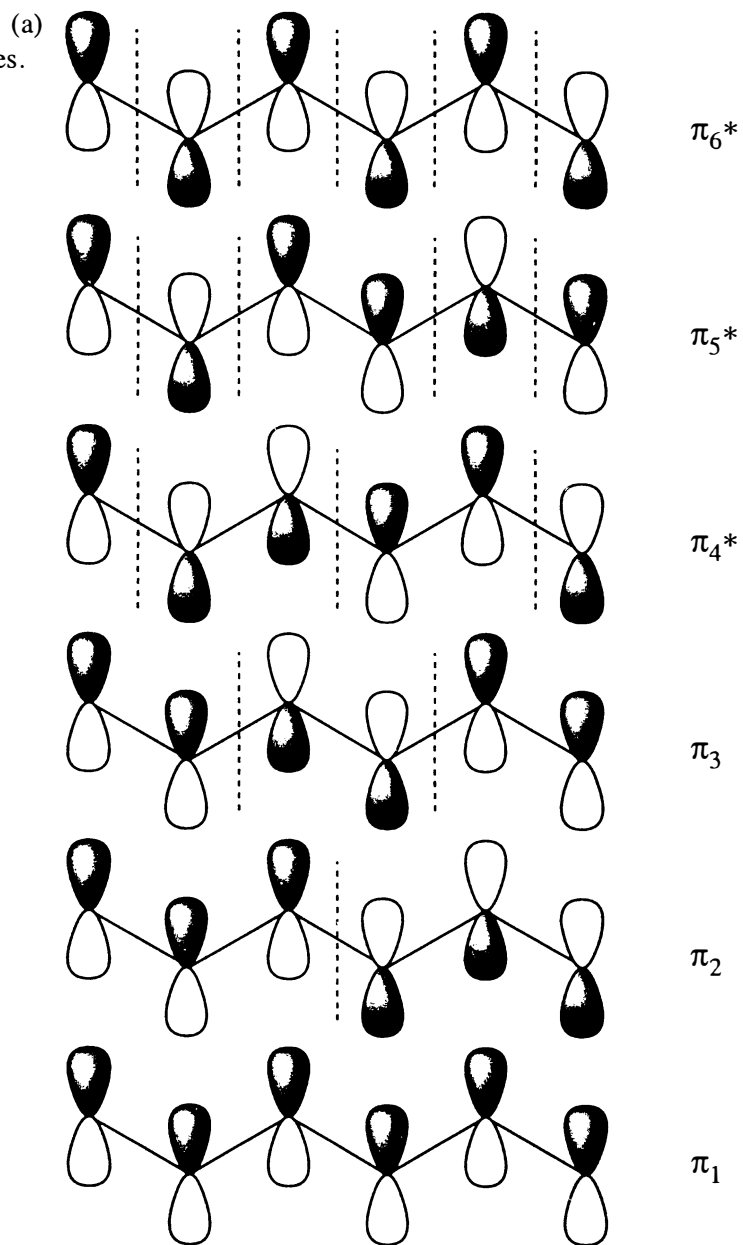
(b) The *endo* isomer is usually preferred because of secondary p orbital overlap of C=O with the diene in the transition state.

(c) The reasoning in (b) applies to stabilization of the transition state of the reaction, not the stability of the product. Arguments based on transition state stability apply to the rate of reaction, inferring that the *endo* product is the kinetic product.

(d) At 25°C, the reaction cannot easily reverse, or at least not very rapidly. The *endo* product is formed faster and is the major product because its transition state is lower in energy—the reaction is under kinetic control. At 90°C, the reverse reaction is not as slow and equilibrium is achieved. The *exo* product is less crowded and therefore more stable—equilibrium control gives the *exo* as the major product.

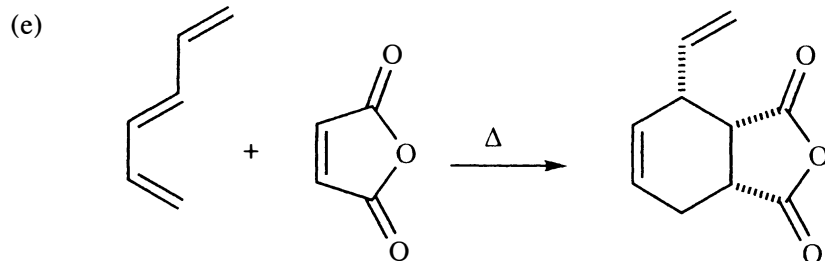
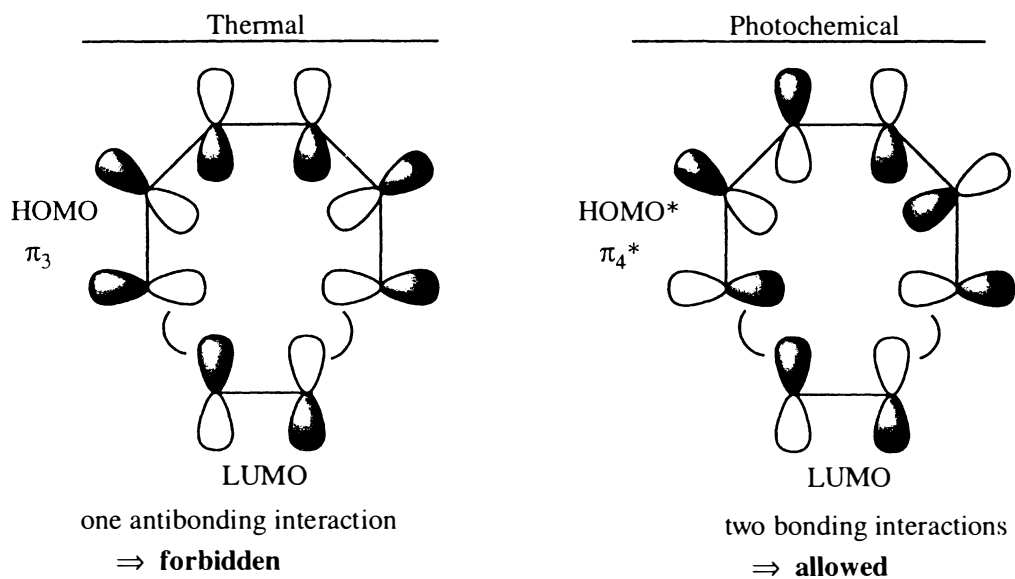


15-35 Nodes are represented by dashed lines.

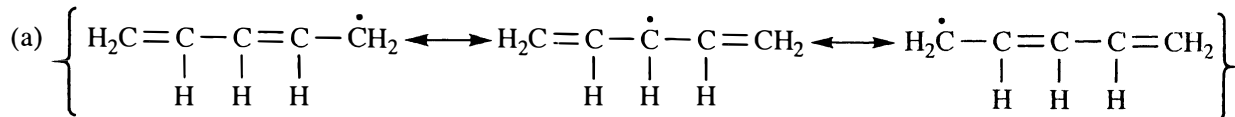


15-35 continued

(d) Whether the triene is the HOMO and the alkene is the LUMO, or *vice versa*, the answer will be the same.



15-36

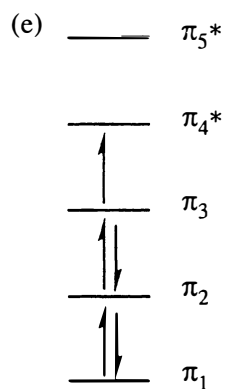
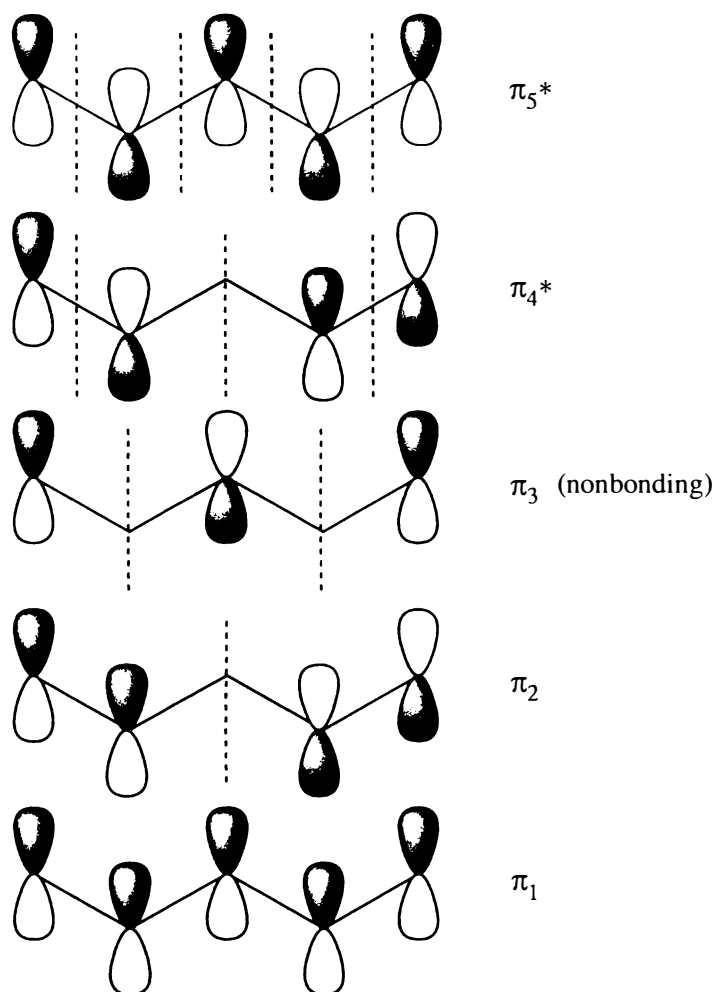


(b) Five atomic orbitals will generate five molecular orbitals.

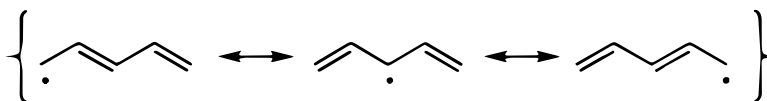
(c) The lowest energy molecular orbital has no nodes. Each higher molecular orbital will have one more node, so the fifth molecular orbital will have four nodes.

15-36 continued

(d) Nodes are represented by dashed lines.



(f) The HOMO, π_3 , contains an unpaired electron giving this species its radical character. The HOMO is a non-bonding orbital with lobes only on carbons 1, 3, and 5, consistent with the resonance picture.



15-36 continued

(g) π_5^*

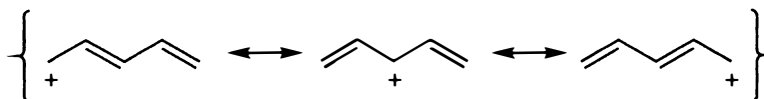
π_4^*

π_3

π_2

π_1

Again, it is π_3 that determines the character of this species. When the single electron in π_3 of the neutral radical is removed, positive charge appears only in the position(s) which that electron occupied. That is, the positive charge depends on the now *empty* π_3 , with *empty* lobes (positive charge) on carbons 1, 3, and 5, consistent with the resonance description.



(h) π_5^*

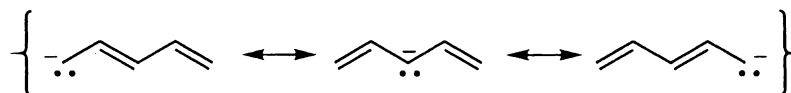
π_4^*

π_3

π_2

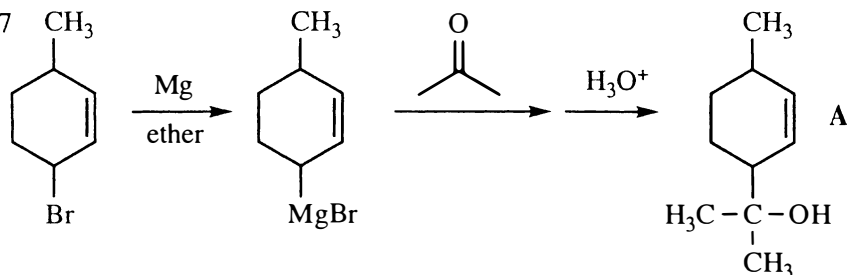
π_1

Again, it is π_3 that determines the character of this species. The negative charge depends on the *filled* π_3 , with lobes (negative charge) on carbons 1, 3, and 5, consistent with the resonance description.

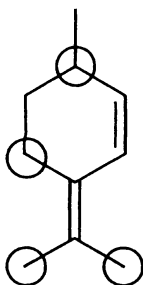


15-37

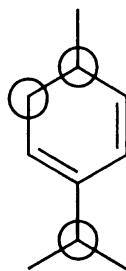
(a)



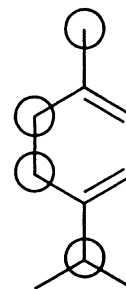
(b) Use Appendix 3 to predict $\lambda_{\max}$ values. Alkyl substituents are circled.



transoid cyclic diene = 217 nm
4 alkyl groups = 20 nm
exocyclic alkene = 5 nm
TOTAL = 242 nm
desired product



cisoid cyclic diene = 253 nm
3 alkyl groups = 15 nm
TOTAL = 268 nm

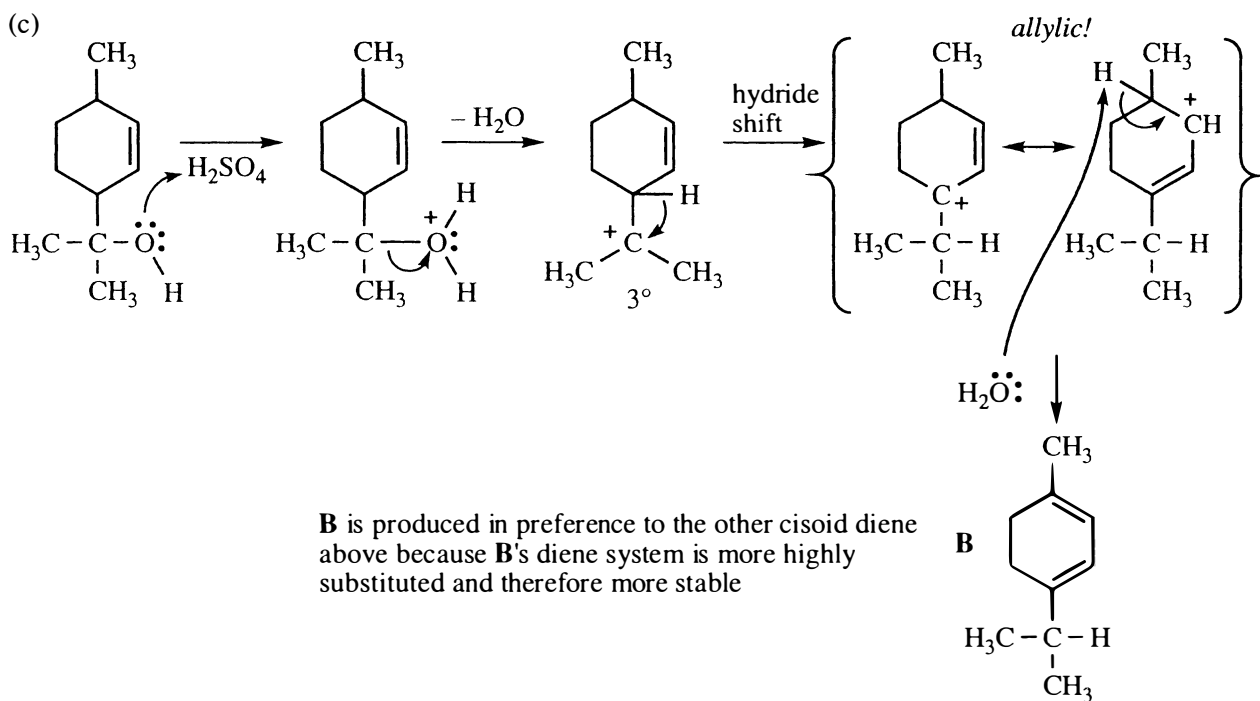


cisoid cyclic diene = 253 nm
4 alkyl groups = 20 nm
TOTAL = 273 nm—AHA!

actual product **B**

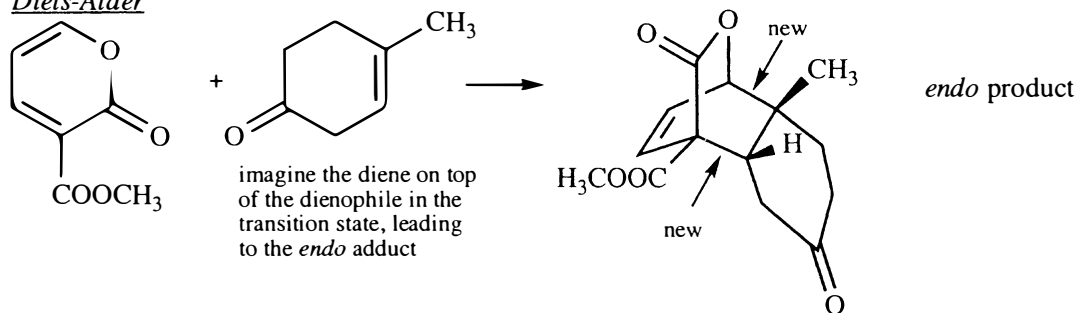
15-37 continued

(c)

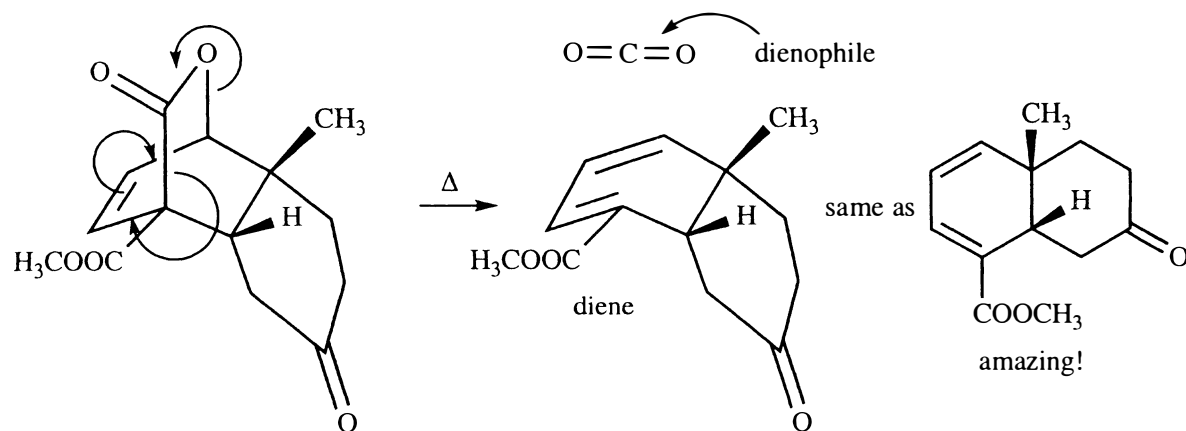


15-38 It is stunningly clever reactions like this that earned E. J. Corey his Nobel Prize.

Diels-Alder

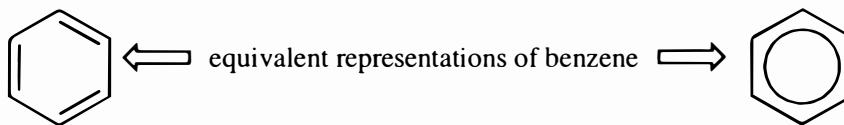


retro-Diels-Alder



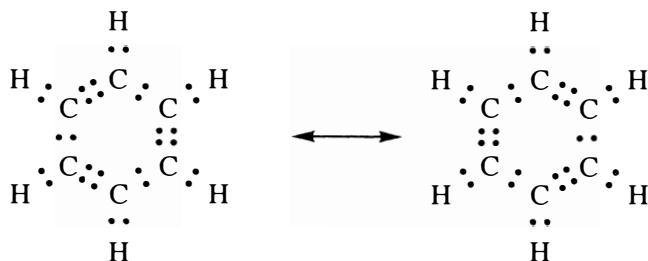
CHAPTER 16—AROMATIC COMPOUNDS

Note: The representation of benzene with a circle to represent the π system is fine for questions of nomenclature, properties, isomers, and reactions. For questions of mechanism or reactivity, however, the representation with three alternating double bonds (the Kekulé picture) is more informative. For clarity and consistency, this Solutions Manual will use the Kekulé form exclusively.



Kekulé form used in
the Solutions Manual

16-1



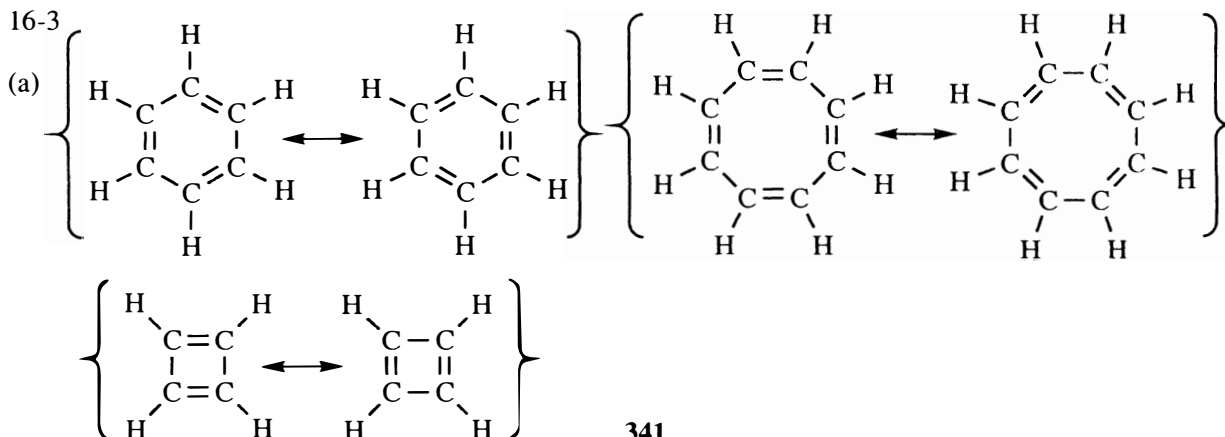
16-2 All values are per mole.

(a)	benzene	– 208 kJ	– 49.8 kcal
	– 1,4-cyclohexadiene	– 240 kJ	– 57.4 kcal
		$\Delta H = + 32 \text{ kJ}$	+ 7.6 kcal

(b)	benzene	– 208 kJ	– 49.8 kcal
	– cyclohexene	– 120 kJ	– 28.6 kcal
		$\Delta H = - 88 \text{ kJ}$	– 21.2 kcal

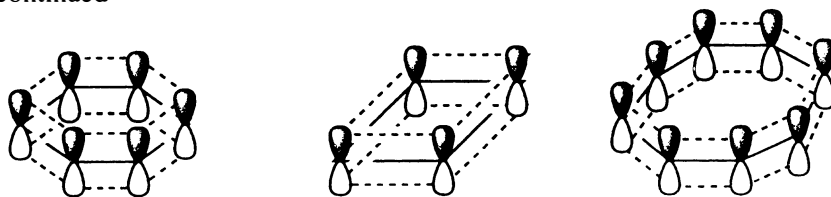
(c)	1,3-cyclohexadiene	– 232 kJ	– 55.4 kcal
	– cyclohexene	– 120 kJ	– 28.6 kcal
		$\Delta H = - 112 \text{ kJ}$	– 26.8 kcal

16-3

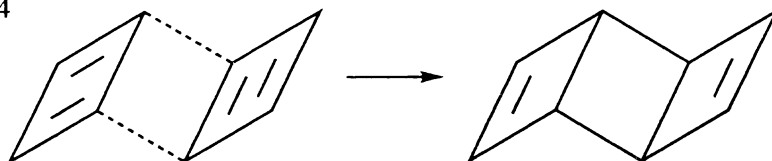


16-3 continued

(b)

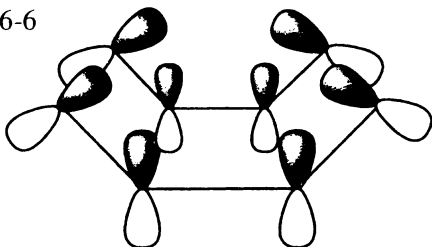


16-4



16-5 Figure 16-8 shows that the first 3 pairs of electrons are in three bonding molecular orbitals of cyclooctatetraene. Electrons 7 and 8, however, are located in two different nonbonding orbitals. As in cyclobutadiene, a planar cyclooctatetraene is predicted to be a diradical, a particularly unstable electron configuration.

16-6



Models show that the angles between p orbitals on adjacent π bonds approach 90° .

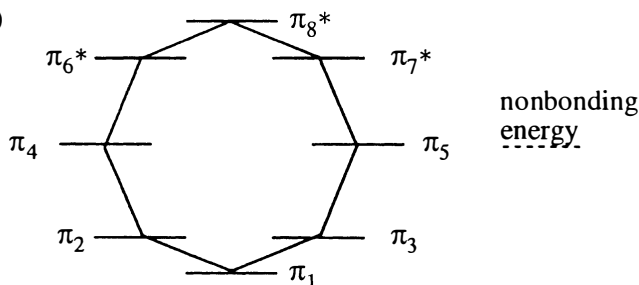
16-7

- (a) nonaromatic: internal hydrogens prevent planarity
- (b) nonaromatic: not all atoms in the ring have a p orbital
- (c) aromatic: [14]annulene
- (d) aromatic: also a [14]annulene in the outer ring: the internal alkene is not part of the aromatic system

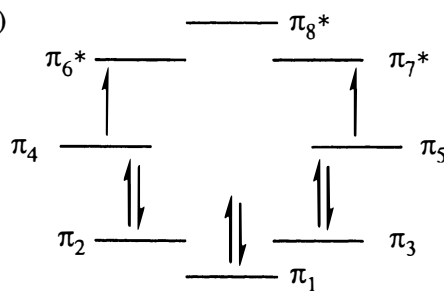
16-8 Azulene satisfies all the criteria for aromaticity, and it has a Huckel number of π electrons: 10. Both heptalene (12 π electrons) and pentalene (8 π electrons) are antiaromatic.

16-9

(a)

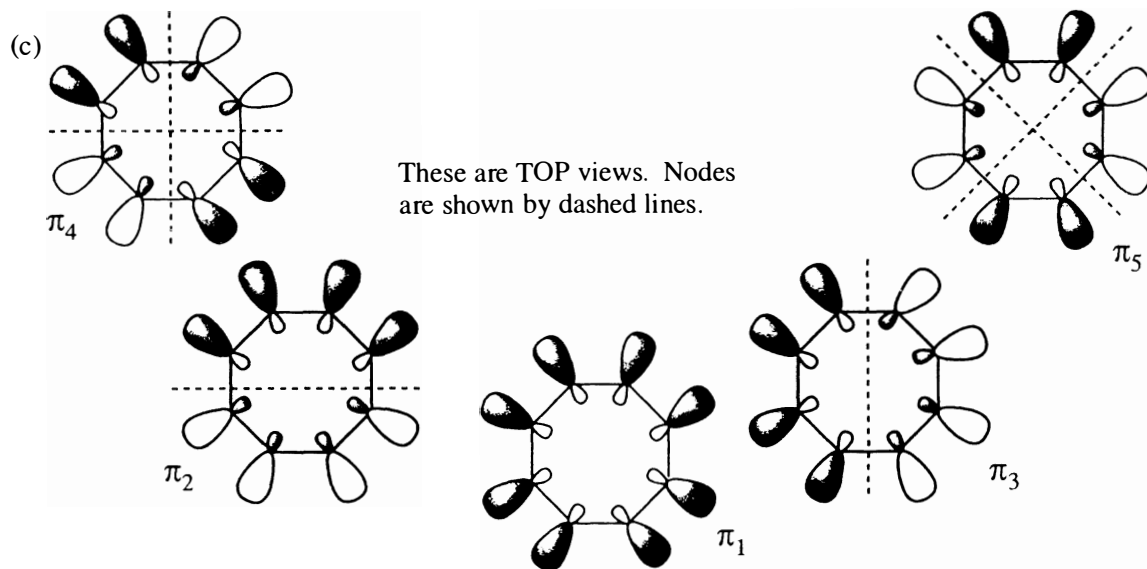


(b)

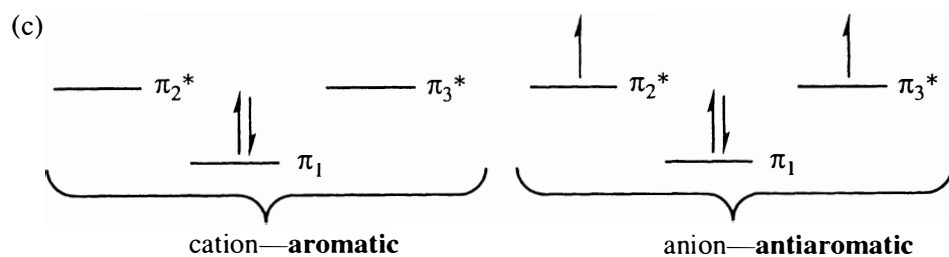
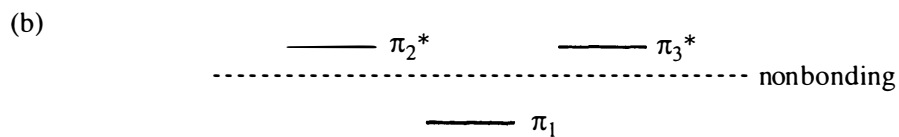
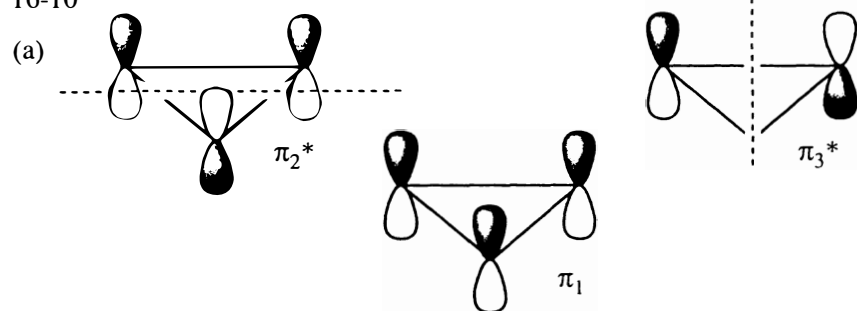


This electronic configuration is antiaromatic.

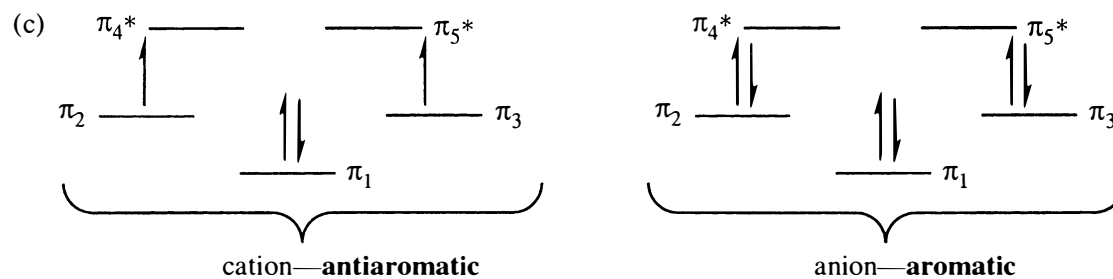
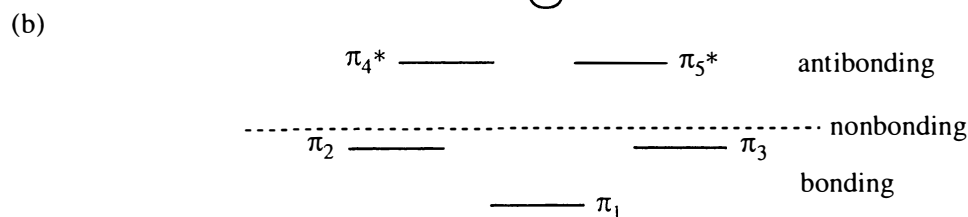
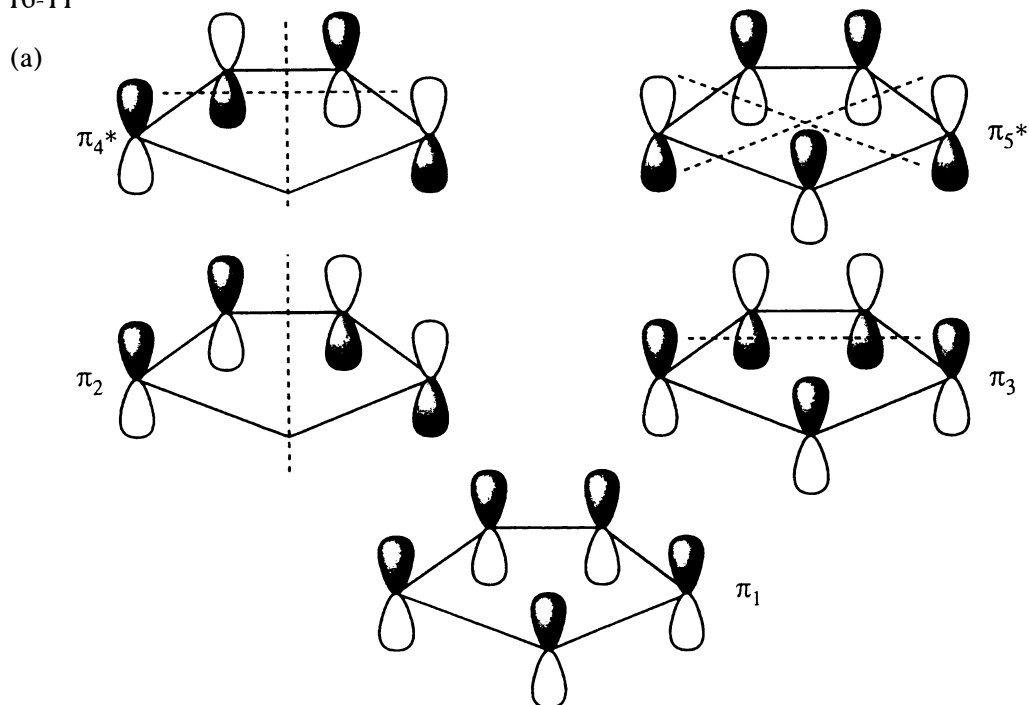
16-9 continued



16-10



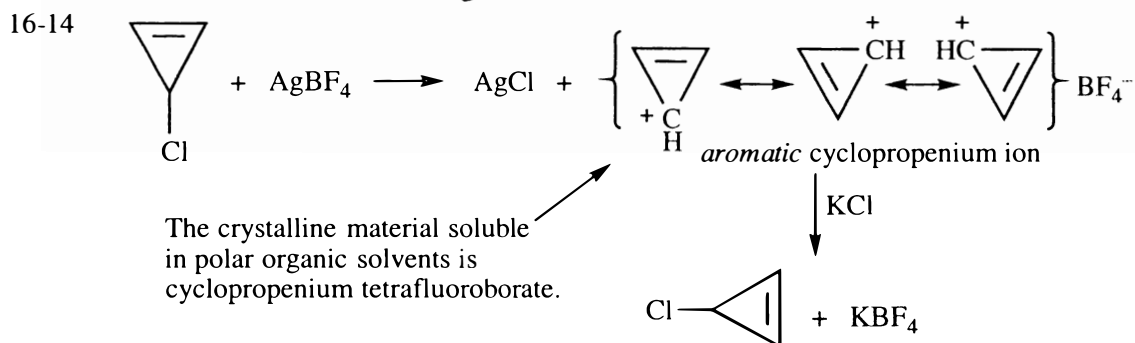
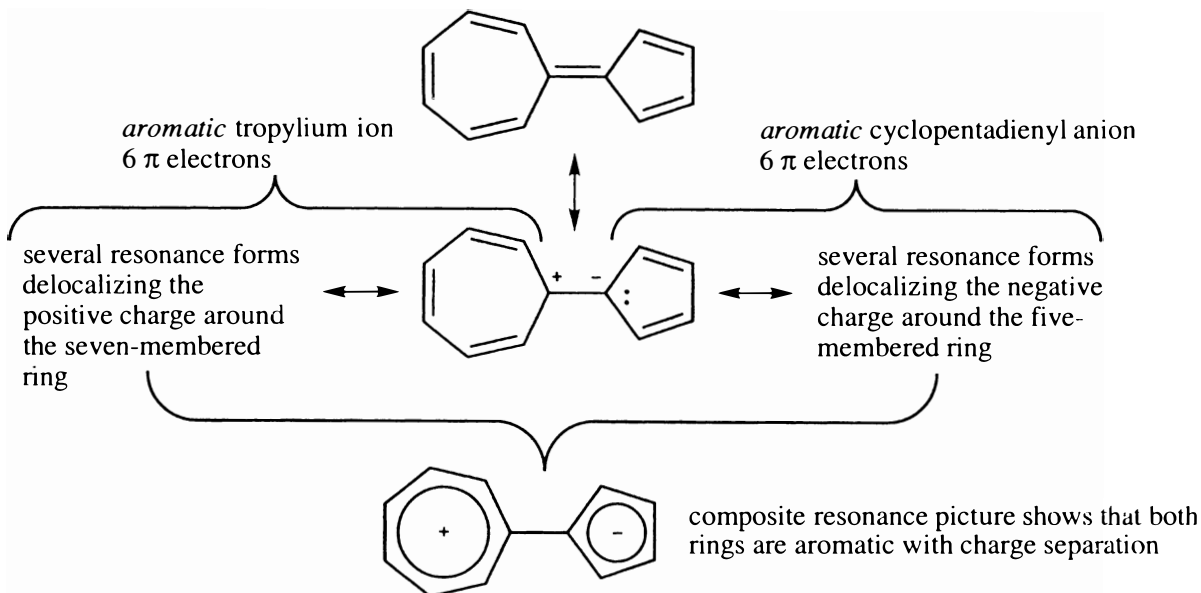
16-11



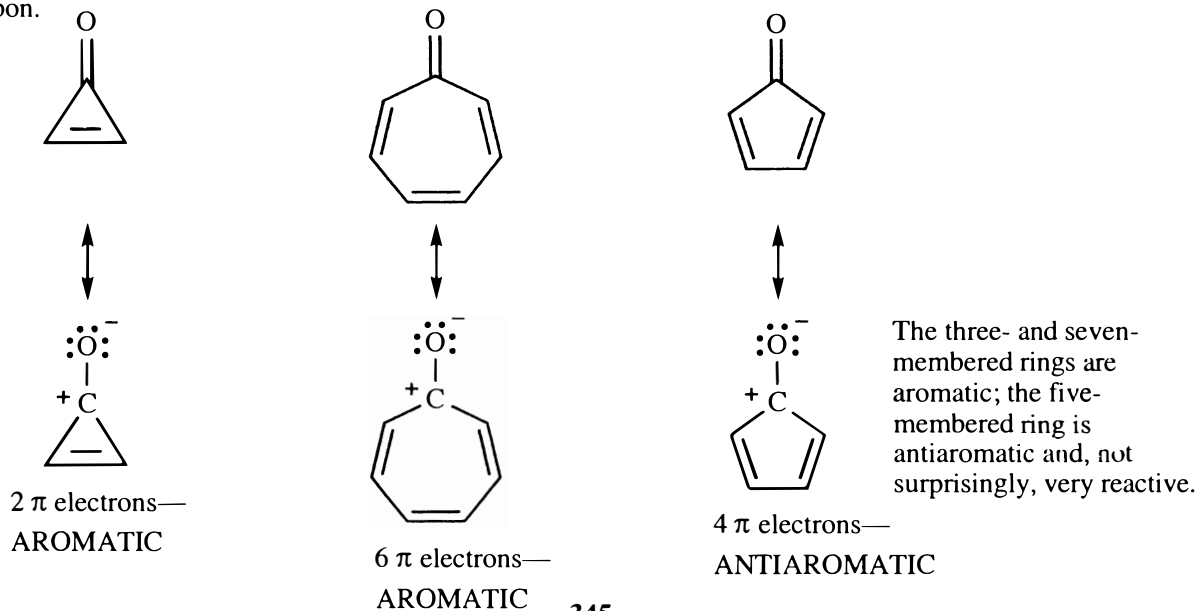
16-12

- (a) antiaromatic: 8 π electrons, not a Huckel number
- (b) aromatic: 10 π electrons, a Huckel number
- (c) aromatic: 18 π electrons, a Huckel number
- (d) antiaromatic: 20 π electrons, not a Huckel number
- (e) nonaromatic: no cyclic π system
- (f) aromatic: 18 π electrons, a Huckel number

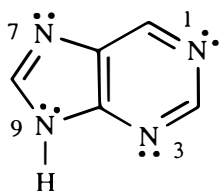
16-13 The reason for the dipole can be seen in a resonance form distributing the electrons to give each ring 6 π electrons. This resonance picture gives one ring a negative charge and the other ring a positive charge.



16-15 Draw resonance forms showing the carbonyl polarization, leaving a positive charge on the carbonyl carbon.



16-16

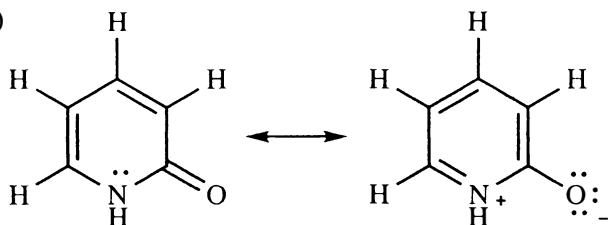


The structure of purine shows two types of nitrogens. One type (N-1, N-3, and N-7) has an electronic structure like the nitrogen in pyridine; the pair of electrons is in an sp^2 orbital planar with the ring. These electrons are available for bonding, and these three nitrogens are basic. The other type of nitrogen at N-9 has an electronic structure like the nitrogen of pyrrole; its electron pair is in a p orbital, perpendicular to the ring system, and more importantly, an essential part of the aromatic pi system. With this pair of electrons, the pi system is aromatic and has 10 electrons, a Hückel number, so the electron pair is not available for bonding and N-9 is not a basic nitrogen.

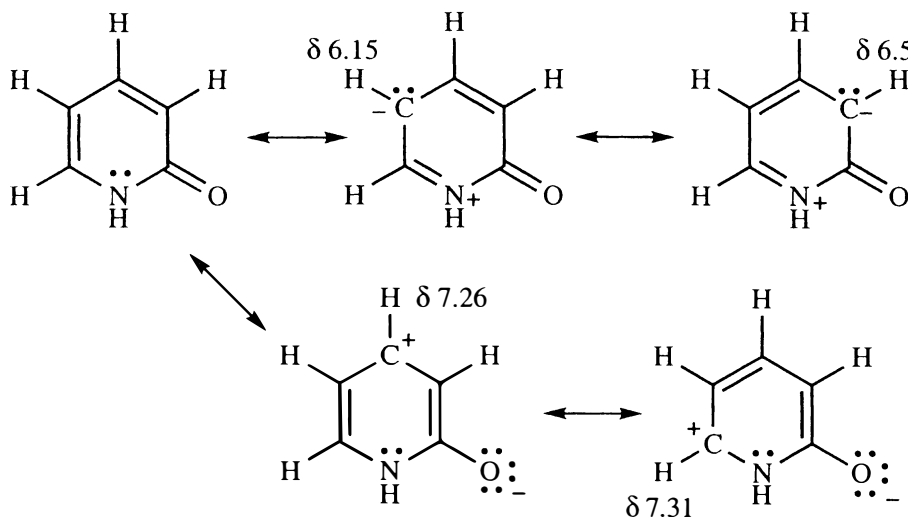
16-17

(a) The proton NMR of benzene shows a single peak at δ 7.2; alkene hydrogens absorb at δ 4.5-6. The chemical shifts of 2-pyridone are more similar to benzene's absorptions than they are to alkenes. It would be correct to infer that 2-pyridone is aromatic.

(b)



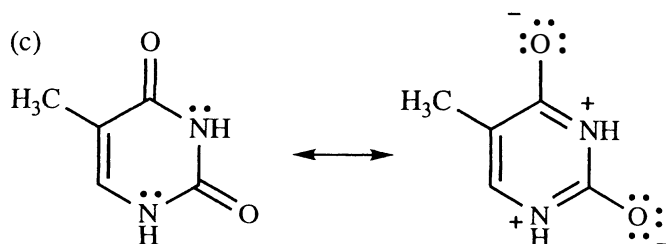
The lone pair of electrons on the nitrogen in the first resonance form is part of the cyclic pi system. The second resonance form shows three alternating double bonds with six electrons in the cyclic pi system, consistent with an aromatic electronic system.



These resonance forms show that the hydrogens at positions with greater electron density are shielded, decreasing chemical shift.

These resonance forms show that the hydrogens at positions with greater positive charge are deshielded, increasing chemical shift.

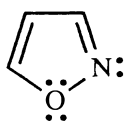
(c)



This resonance form of thymine shows a cyclic pi system with 6 pi electrons, consistent with an aromatic system. Four of these electrons came from the two lone pairs of electrons on nitrogens in the first resonance form.

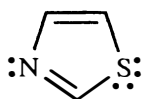
16-18

(a)



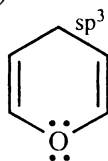
aromatic: 4 π electrons in double bonds plus one pair from oxygen

(b)



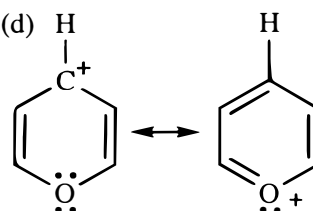
aromatic: 4 π electrons in double bonds plus one pair from sulfur

(c)



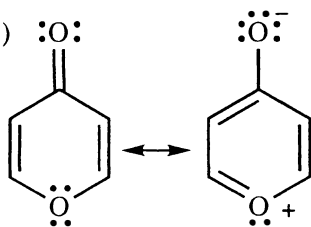
not aromatic: no cyclic π system because of sp^3 carbon

(d)



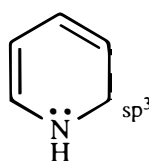
aromatic: cation on carbon-4 indicates an empty p orbital; two π bonds plus a pair of electrons from oxygen makes a 6 π electron system

(e)



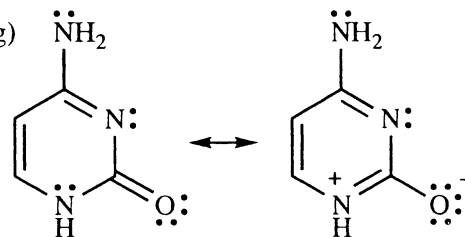
aromatic: resonance form shows "push-pull" of electrons from one O to the other, making a cyclic π system with 6 electrons

(f)



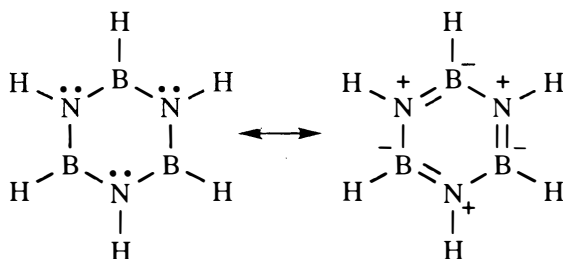
not aromatic: no cyclic π system because of sp^3 carbon

(g)



aromatic: resonance form shows electron pair from N making a cyclic π system with 6 electrons

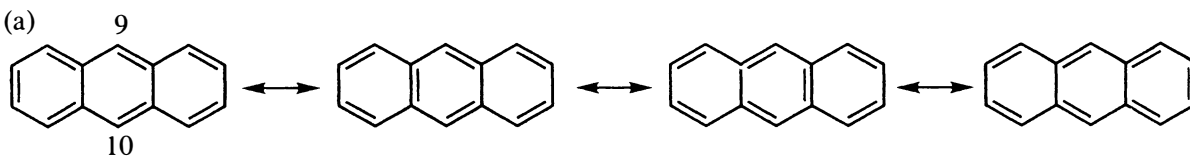
16-19



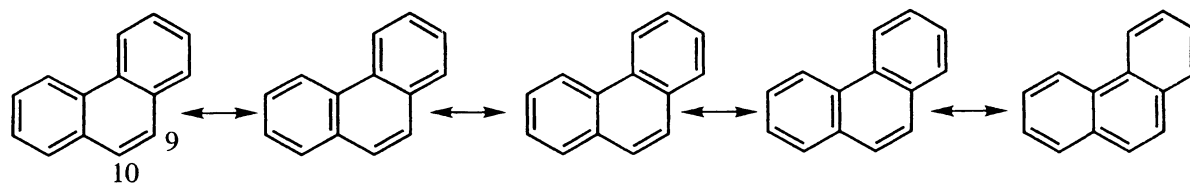
Borazole is a non-carbon equivalent of benzene. Each boron is hybridized in its normal sp^2 . Each nitrogen is also sp^2 with its pair of electrons in its p orbital. The system has six π electrons in 6 p orbitals—aromatic!

16-20

(a)



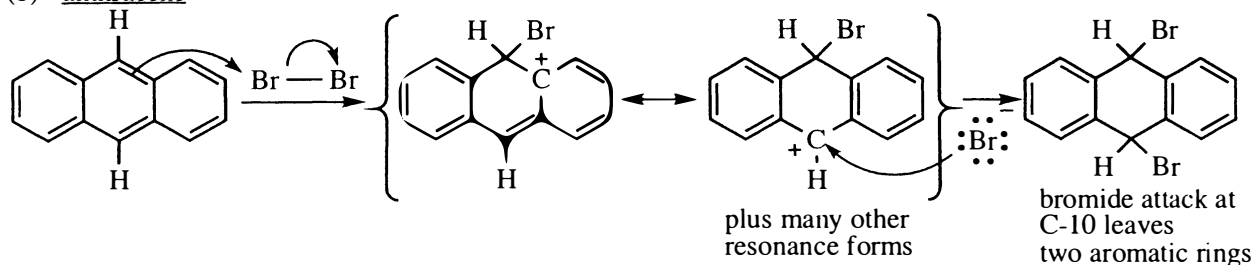
anthracene



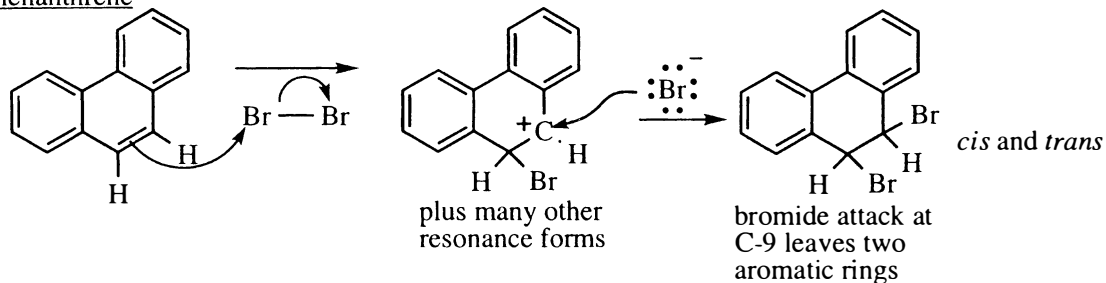
phenanthrene

16-20 continued

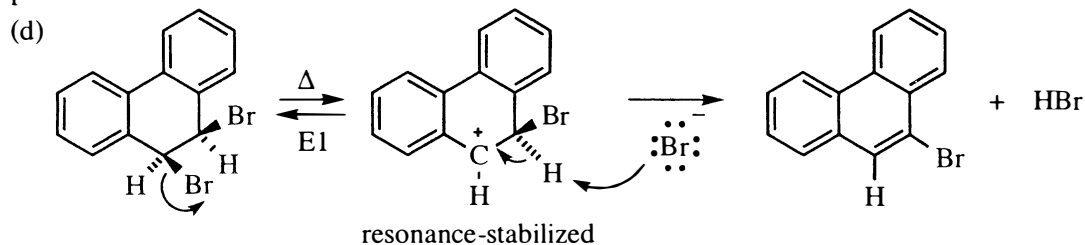
(b) anthracene



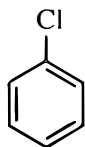
phenanthrene



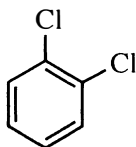
(c) A typical addition of bromine occurs with a bromonium ion intermediate which can give only anti addition. Addition of bromine to phenanthrene, however, generates a free carbocation because the carbocation is benzylic, stabilized by resonance over two rings. In the second step of the mechanism, bromide nucleophile can attack either side of the carbocation giving a mixture of *cis* and *trans* products.



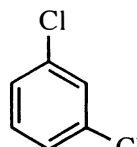
16-21



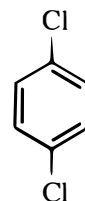
chlorobenzene



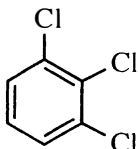
o-dichlorobenzene
(1,2-dichlorobenzene)



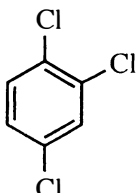
m-dichlorobenzene
(1,3-dichlorobenzene)



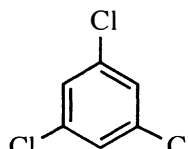
p-dichlorobenzene
(1,4-dichlorobenzene)



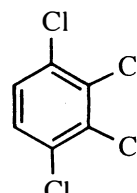
1,2,3-trichlorobenzene



1,2,4-trichlorobenzene

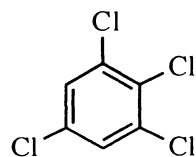


1,3,5-trichlorobenzene

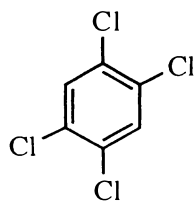


1,2,3,4-tetrachloro-
benzene

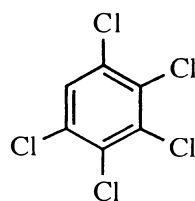
16-21 continued



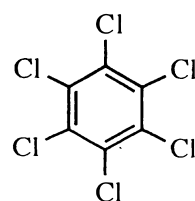
1,2,3,5-tetrachlorobenzene



1,2,4,5-tetrachlorobenzene



1,2,3,4,5-pentachlorobenzene



1,2,3,4,5,6-hexachlorobenzene

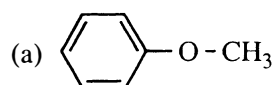
16-22

- (a) fluorobenzene
(b) 4-phenylbut-1-yne
(c) *m*-methylphenol, or 3-methylphenol
(common name: *m*-cresol)

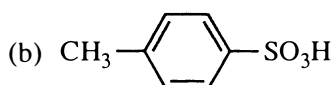
- (d) *o*-nitrostyrene
(e) *p*-bromobenzoic acid, or 4-bromobenzoic acid
(f) isopropoxybenzene, or isopropyl phenyl ether

- (g) 3,4-dinitrophenol
(h) benzyl ethyl ether, or benzoxyethane, or (ethoxymethyl)benzene, or α -ethoxytoluene

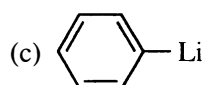
16-23 These examples are representative. Your examples may be different from these and still be correct.



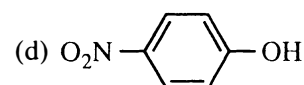
methyl phenyl ether
or methoxybenzene
or anisole



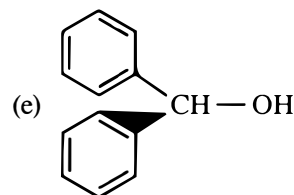
p-toluenesulfonic acid



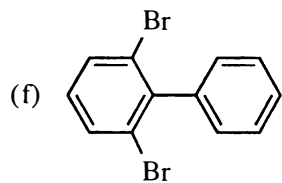
phenyllithium



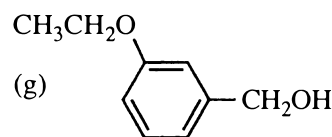
These are *phenols*.
This is 4-nitrophenol.



diphenylmethanol

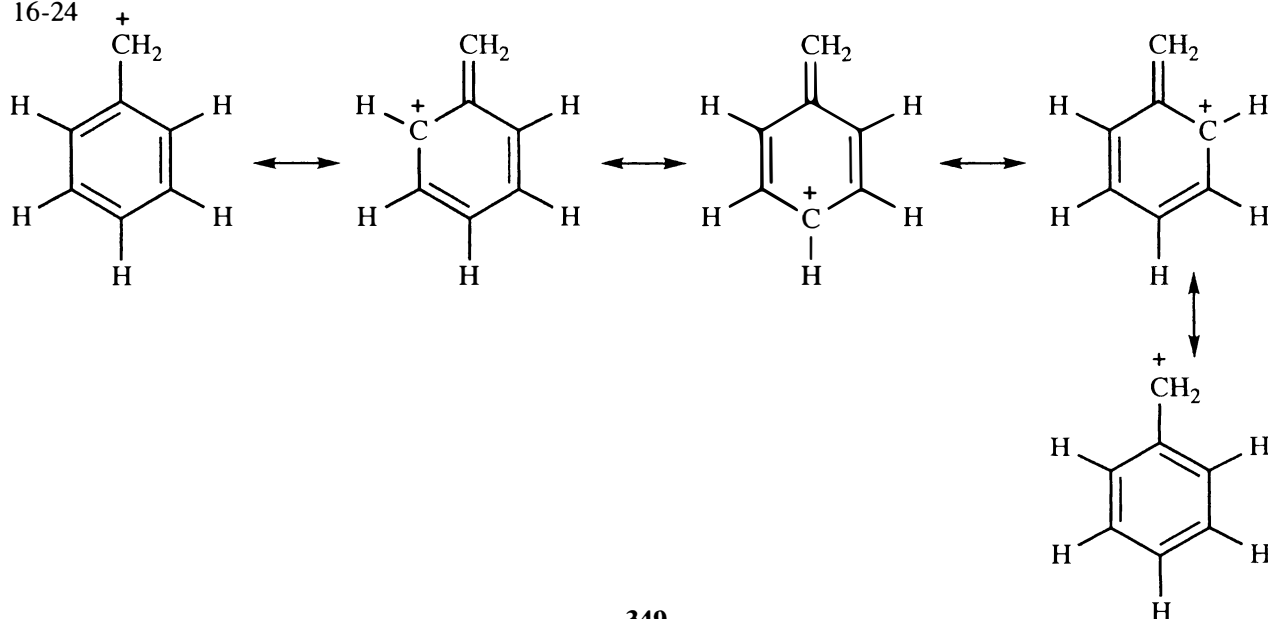


1,3-dibromo-2-phenylbenzene

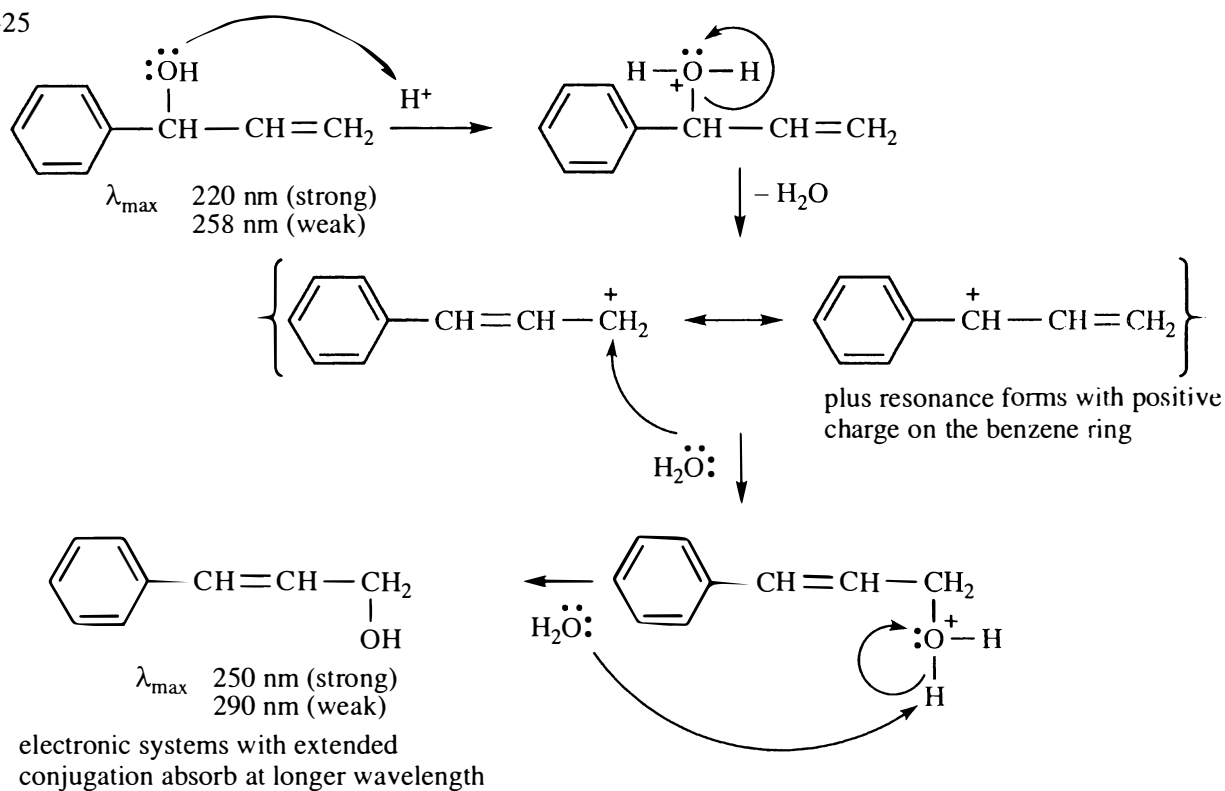


3-ethoxybenzyl alcohol
or 3-ethoxyphenylmethanol

16-24

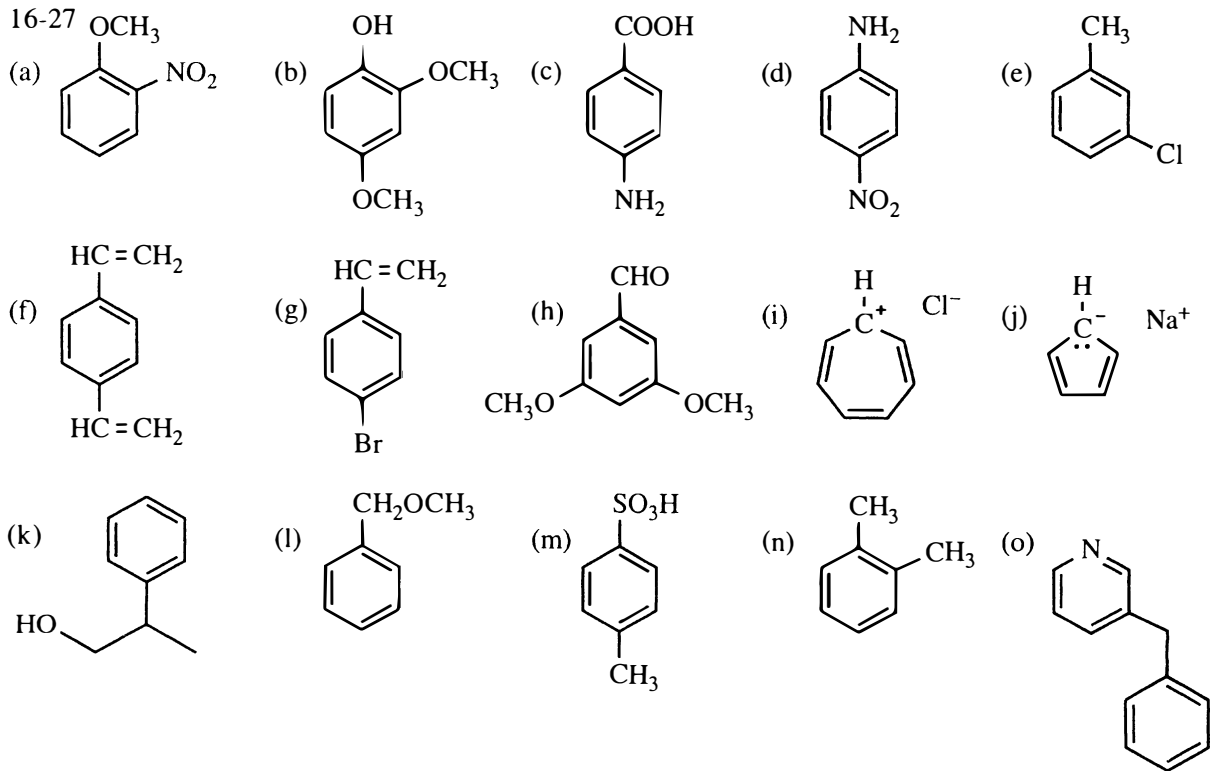


16-25



16-26 Please refer to solution 1-20, page 12 of this Solutions Manual.

16-27

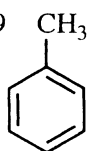


16-28

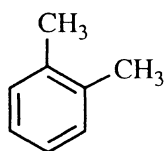
- (a) 1,2-dichlorobenzene (*ortho*)
 (b) 4-nitroanisole (*para*)
 (c) 2,3-dibromobenzoic acid
 (d) 2,7-dimethoxynaphthalene

- (e) 3-chlorobenzoic acid (*meta*)
 (f) 2,4,6-trichlorophenol
 (g) 2-*sec*-butylbenzaldehyde (*ortho*)
 (h) cyclopropenium tetrafluoroborate

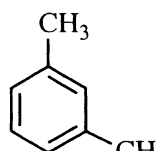
16-29



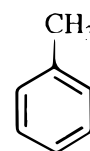
toluene



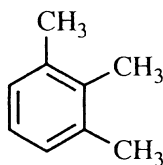
o-xylene



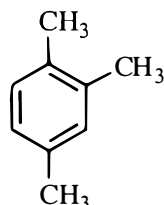
m-xylene



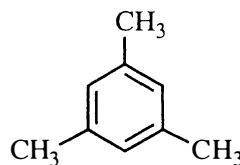
p-xylene



1,2,3-trimethylbenzene



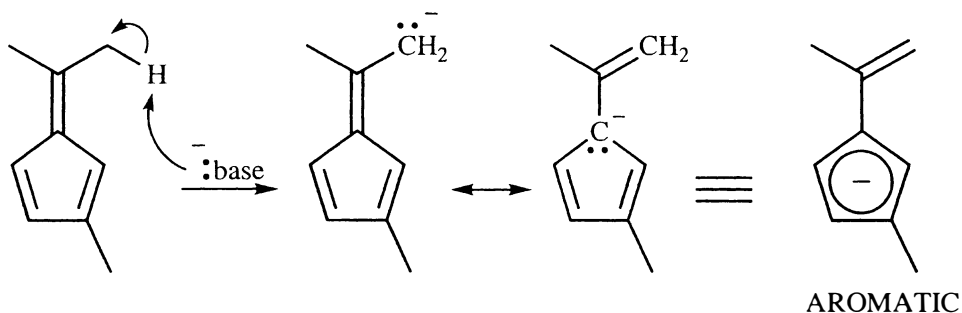
1,2,4-trimethylbenzene



1,3,5-trimethylbenzene
(common name: mesitylene)

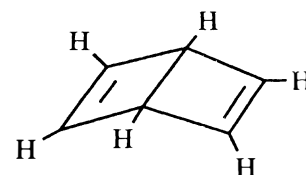
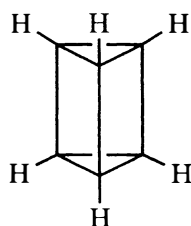
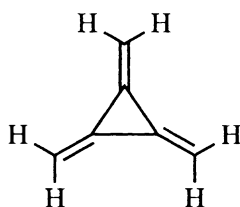
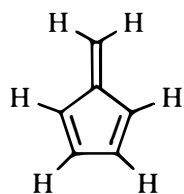
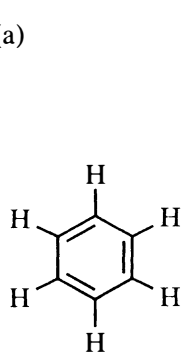
16-30 Aromaticity is one of the strongest stabilizing forces in organic molecules. The cyclopentadienyl system is stabilized in the anion form where it has 6 π electrons, a Huckel number. The question then becomes: which of the four structures can lose a proton to become aromatic?

While the first, third, and fourth structures can lose protons from sp^3 carbons to give resonance-stabilized anions, only the second structure can make a cyclopentadienide anion. It will lose a proton most easily of these four structures which, by definition, means it is the strongest acid.

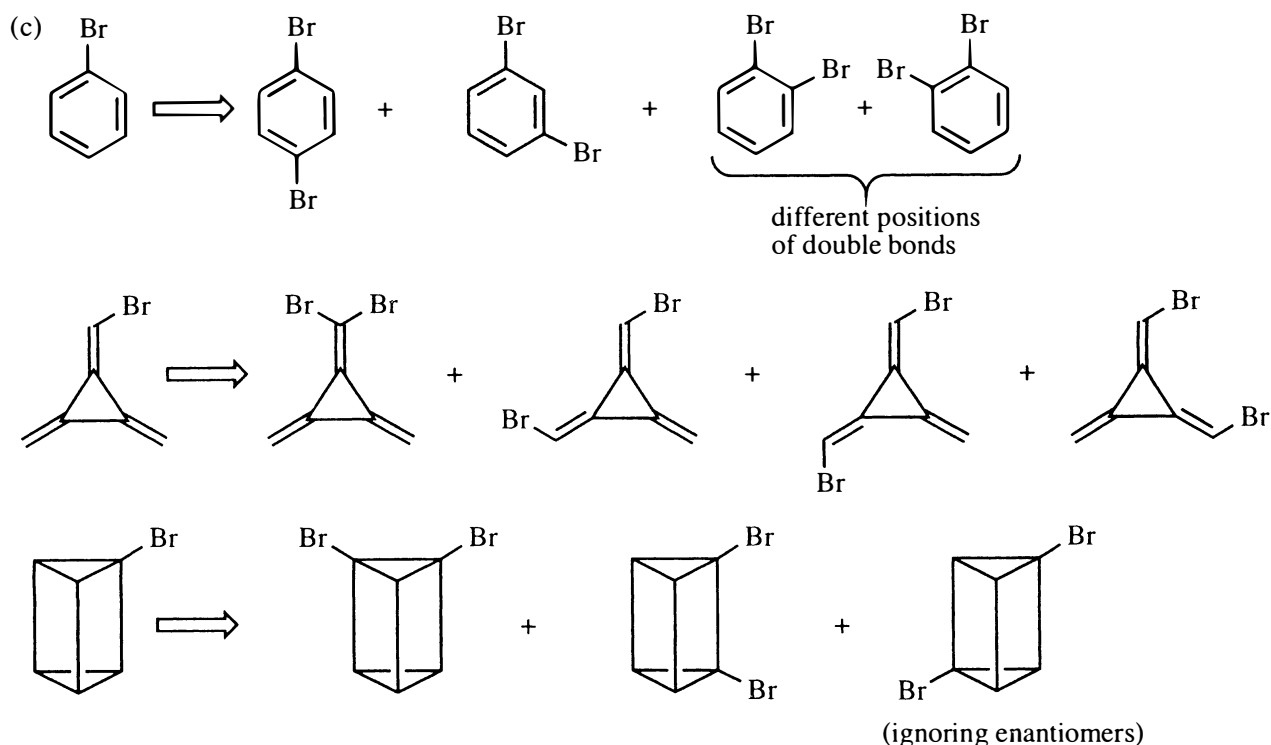
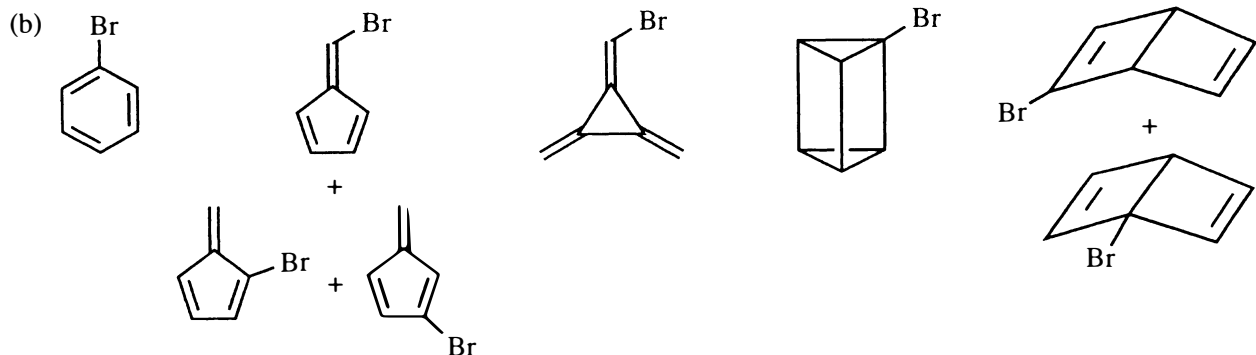


16-31

(a)



16-31 continued

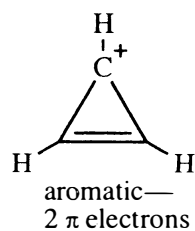
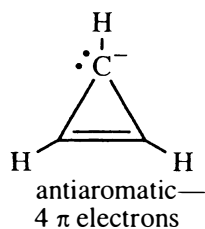
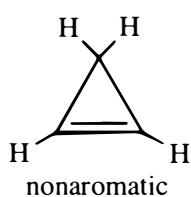


(d) The only structure consistent with three isomers of dibromobenzene is the prism structure, called Ladenburg benzene. It also gives no test for alkenes, consistent with the behavior of benzene. (Kekulé defended his structure by claiming that the "two" structures of *ortho*-dibromobenzene were rapidly interconverted, equilibrating so quickly that they could never be separated.)

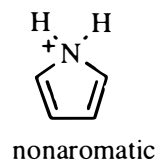
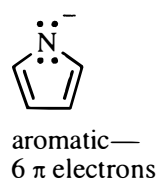
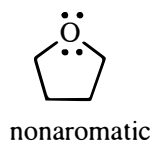
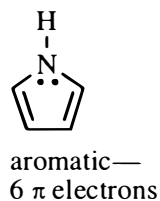
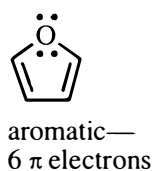
(e) We now know that three- and four-membered rings are the least stable, but this fact was unknown to chemists during the mid-1800s when the benzene controversy was raging. Ladenburg benzene has two three-membered rings and three four-membered rings (of which only four of the rings are independent), which we would predict to be unstable. (In fact, the structure has been synthesized. Called *prismane*, it is NOT aromatic, but rather, is very reactive toward addition reactions.)

16-32

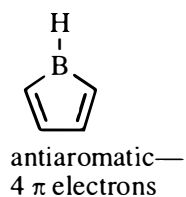
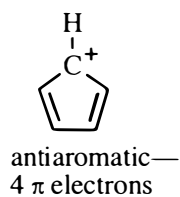
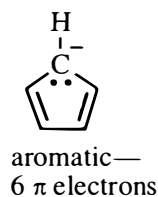
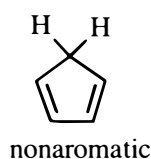
(a)



(b)

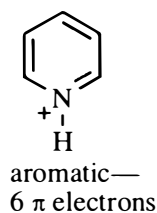
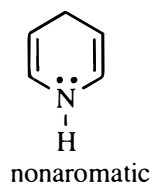
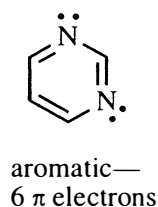
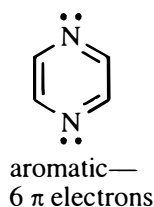


(c)

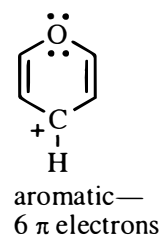
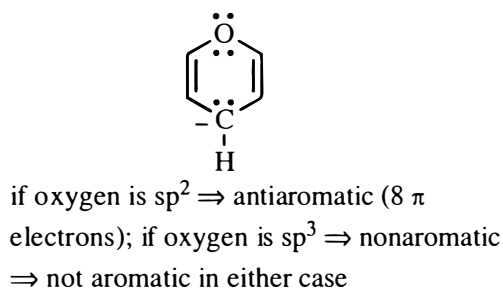
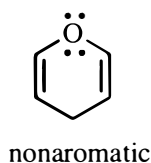


(B is sp^2 , but donates
no electrons to the π
system)

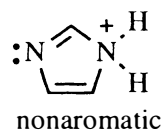
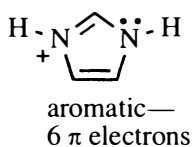
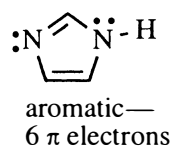
(d)



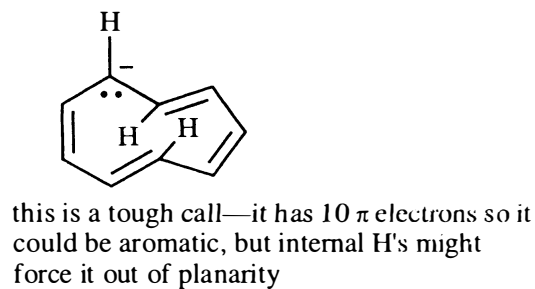
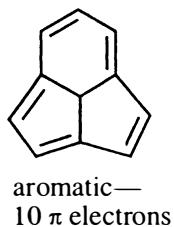
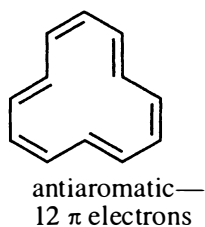
(e)



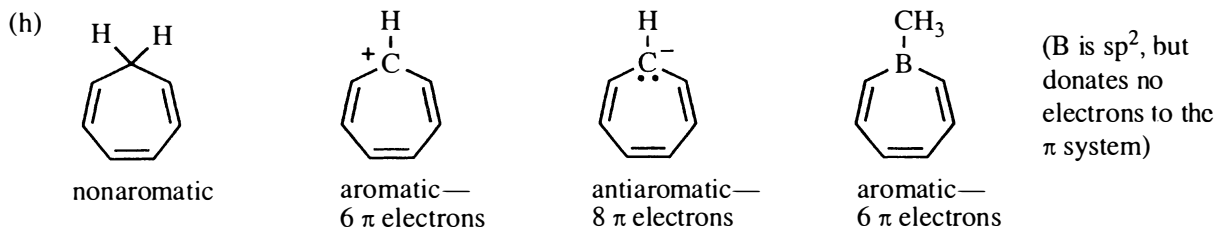
(f)



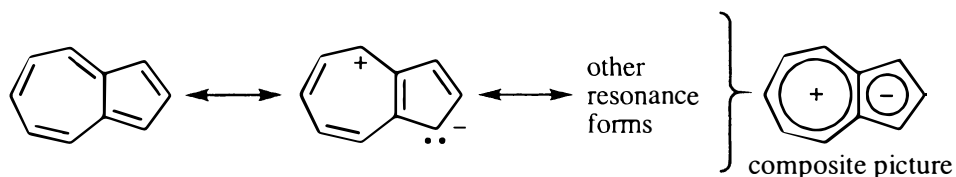
(g)



16-32 continued

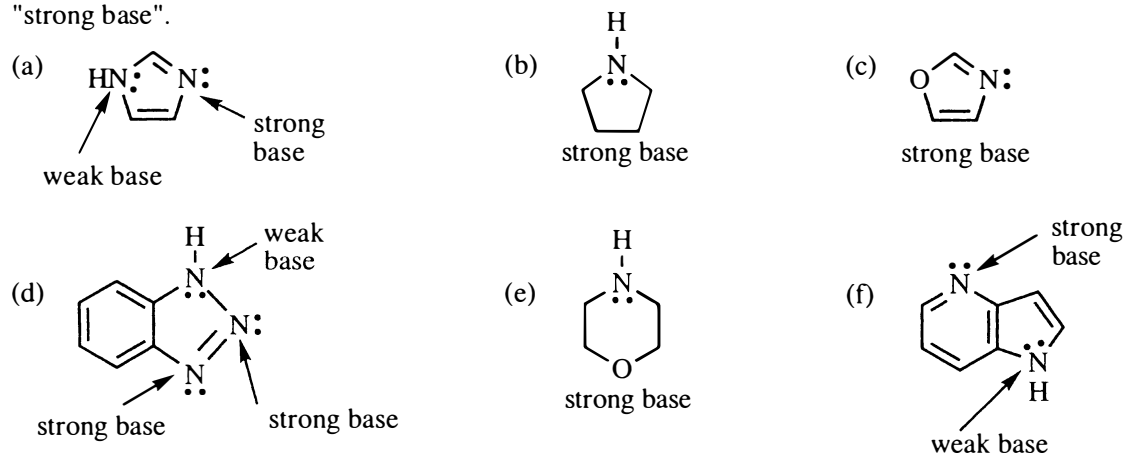


16-33 The clue to azulene is recognition of the five- and seven-membered rings. To attain aromaticity, a seven-membered carbon ring must have a positive charge; a five-membered carbon ring must have a negative charge. Drawing a resonance form of azulene shows this:

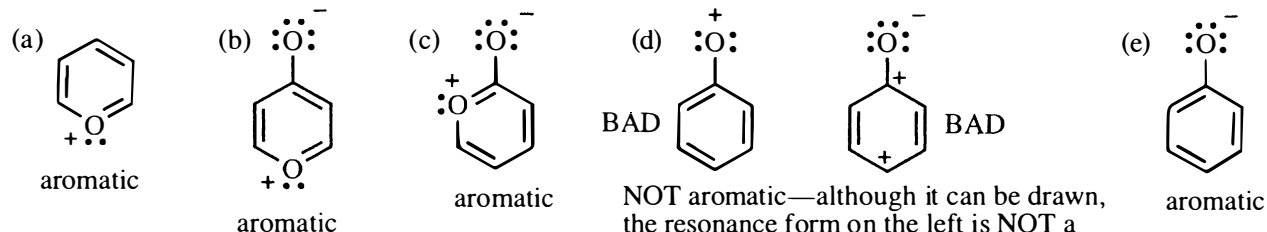


The composite picture shows that the negative charge is concentrated in the five-membered ring, giving rise to the dipole.

16-34 Whether a nitrogen is strongly basic or weakly basic depends on the location of its electron pair. If the electron pair is needed for an aromatic π system, the nitrogen will not be basic (shown here as "weak base"). If the electron pair is in either an sp^2 or sp^3 orbital, it is available for bonding, and the nitrogen is a "strong base".



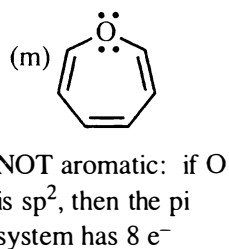
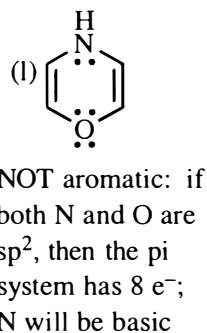
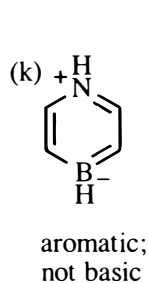
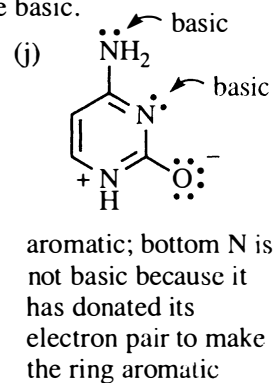
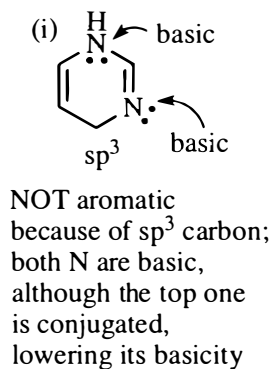
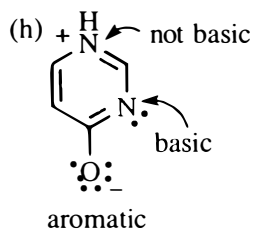
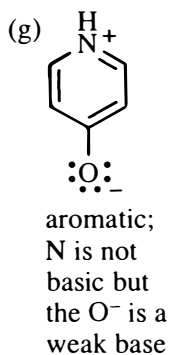
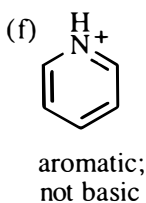
16-35 Where a resonance form demonstrates aromaticity, the resonance form is shown.



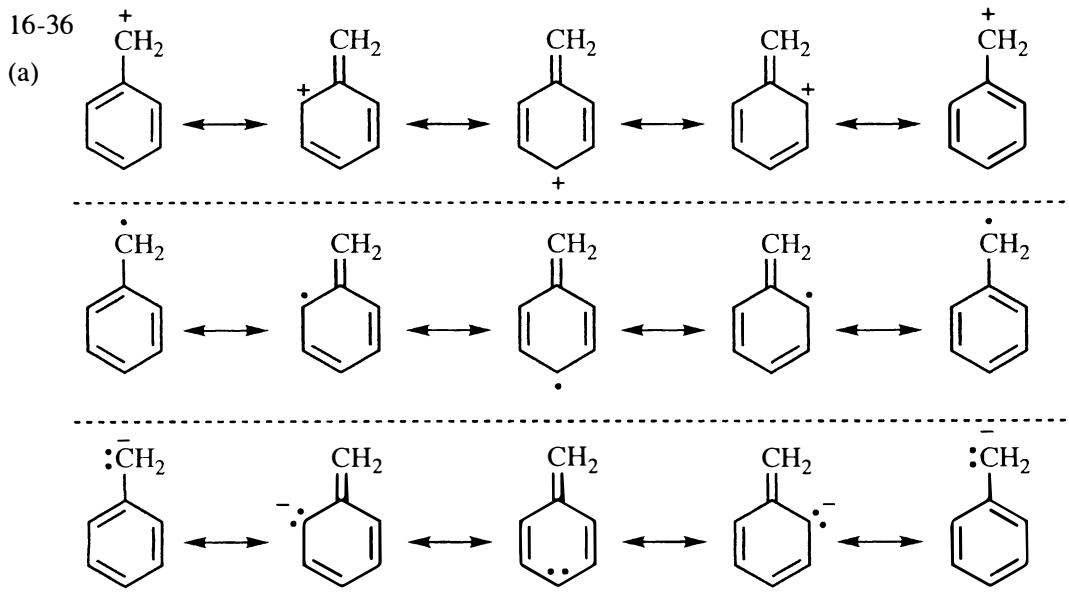
NOT aromatic—although it can be drawn, the resonance form on the left is NOT a significant contributor because the oxygen does not have a full octet; the form on the right shows the correct polarization of the carbonyl, but it's still not aromatic because of only 4 π electrons

16-35 continued

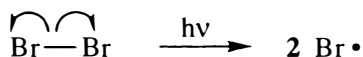
Nitrogens whose electrons are needed to complete the aromatic π system will not be basic.



16-36

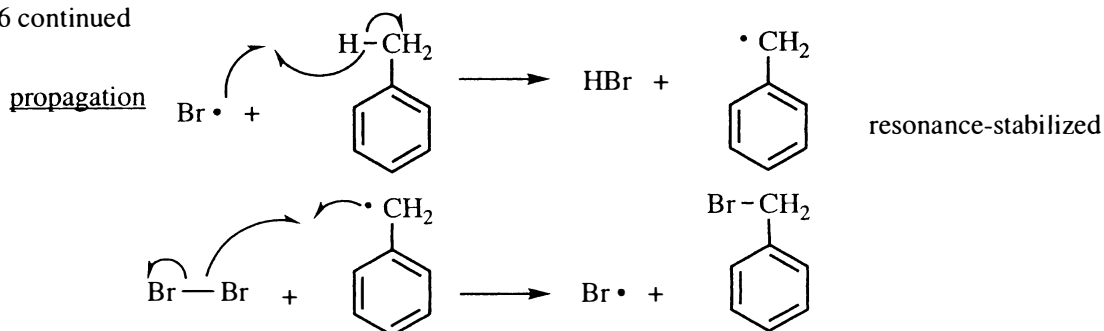


(b) initiation

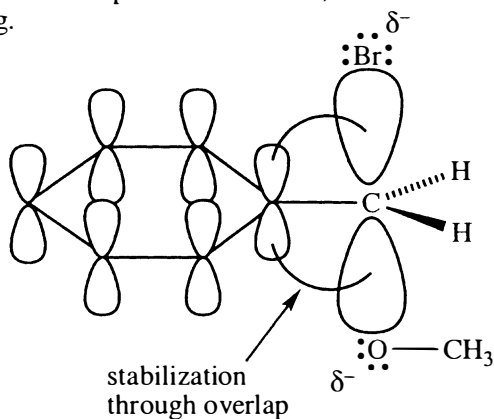


propagation steps on the next page

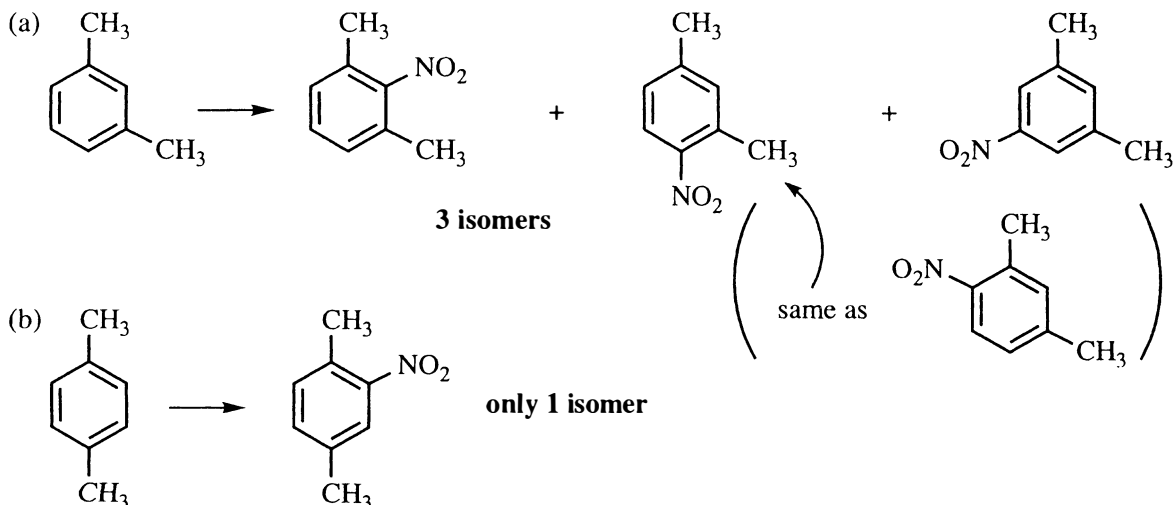
16-36 continued



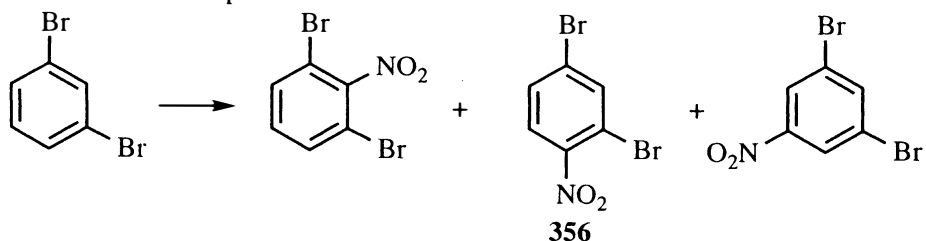
(c) Both reactions are S_N2 on primary carbons, but the one at the benzylic carbon occurs faster. In the transition state of S_N2 , as the nucleophile is approaching the carbon and the leaving group is departing, the electron density resembles that of a p orbital. As such, it can be stabilized through overlap with the π system of the benzene ring.



16-37

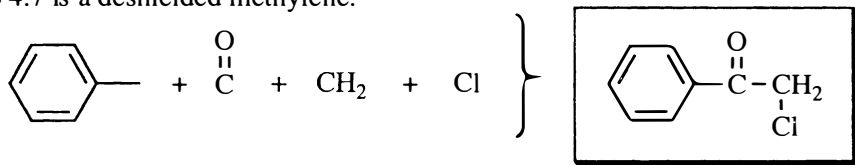


(c) The original compound had to have been *meta*-dibromobenzene as this is the only dibromo isomer that gives three mononitrated products.

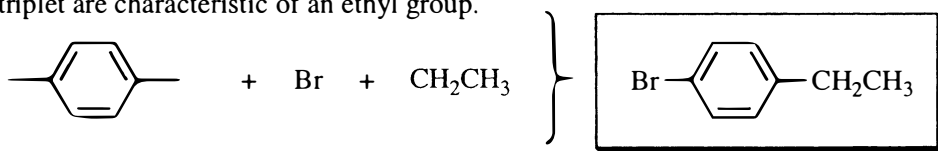


16-38

(a) The formula C_8H_7OCl has five elements of unsaturation, probably a benzene ring (4) plus either a double bond or a ring. The IR suggests a conjugated carbonyl at 1690 cm^{-1} and an aromatic ring at 1602 cm^{-1} . The NMR shows a total of five aromatic protons, indicating a monosubstituted benzene. A 2H singlet at $\delta\ 4.7$ is a deshielded methylene.



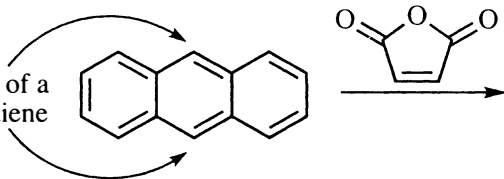
(b) The mass spectral evidence of molecular ion peaks of 1 : 1 intensity at 184 and 186 shows the presence of a bromine atom. The m/z 184 minus 79 for bromine gives a mass of 105 for the rest of the molecule, which is about a benzene ring plus two carbons and a few hydrogens. The NMR shows four aromatic hydrogens in a typical *para* pattern (two doublets), indicating a *para*-disubstituted benzene. The 2H quartet and 3H triplet are characteristic of an ethyl group.



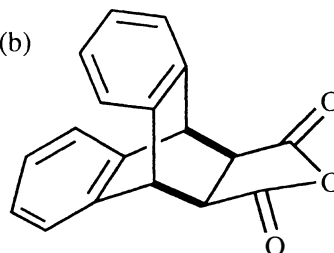
16-39

(a)

like the ends of a
conjugated diene



(b)



Diels-Alder
product

new sigma bonds shown in bold

16-40

(a) No, biphenyl is not fused. The rings must share two atoms to be labeled "fused".

(b) There are 12 π electrons in biphenyl compared with 10 for naphthalene.

(c) Biphenyl has 6 "double bonds". An isolated alkene releases 120 kJ/mole upon hydrogenation.

predicted: $6 \times 120\text{ kJ/mole}$ (28.6 kcal/mole) $\approx 720\text{ kJ/mole}$ (172 kcal/mole)

observed:

418 kJ/mole (100 kcal/mole)

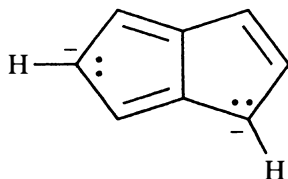
resonance energy:

302 kJ/mole (72 kcal/mole)

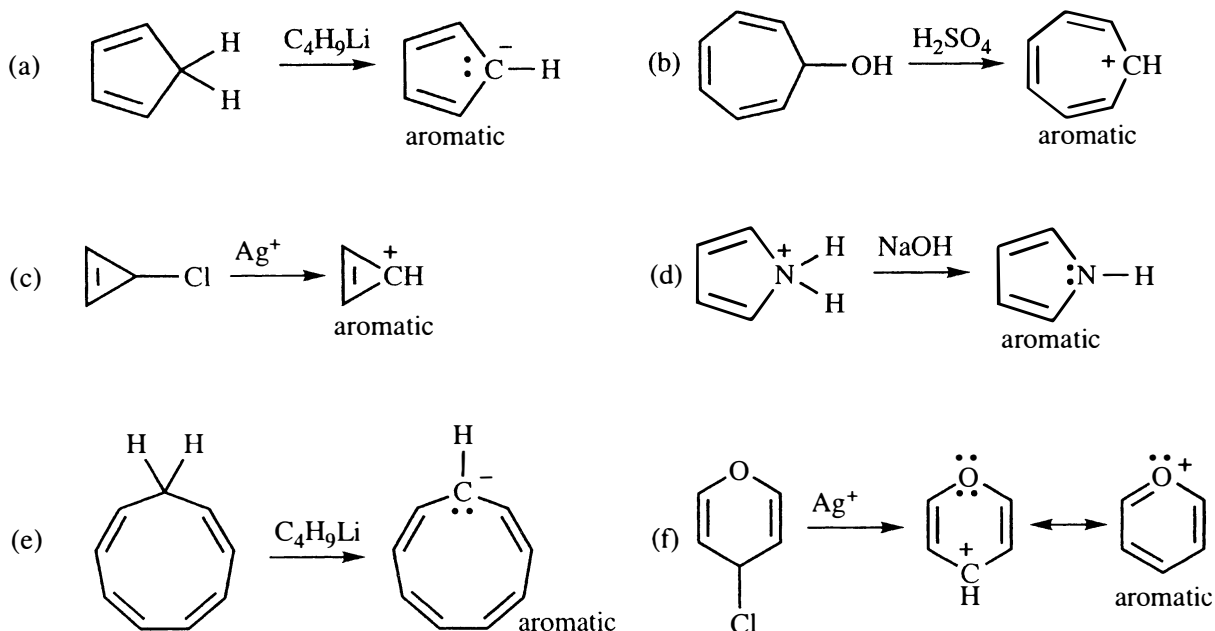
(d) On a "per ring" basis, biphenyl is $302 \div 2 = 151\text{ kJ/mole}$, the same as the value for benzene.

Naphthalene's resonance energy is 252 kJ/mole (60 kcal/mole); on a "per ring" basis, naphthalene has only 126 kJ/mole of stabilization per ring. This is consistent with the greater reactivity of naphthalene compared with benzene. In fact, the more fused rings, the lower the resonance energy per ring, and the more reactive the compound. (Refer to Problem 16-20.)

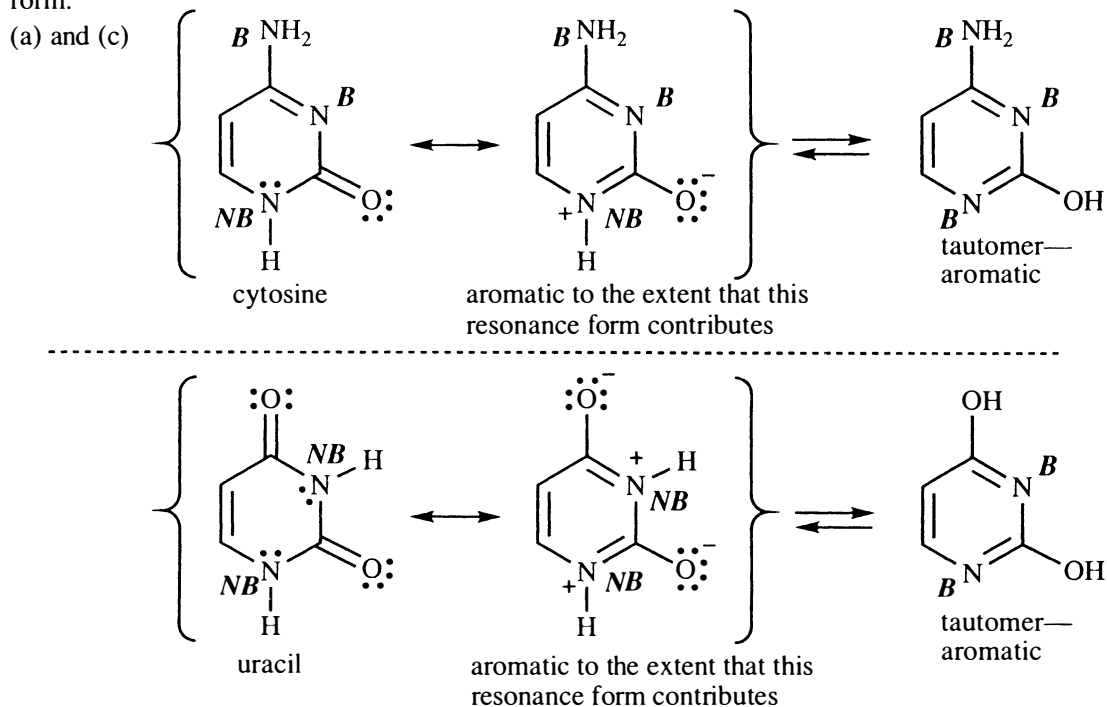
16-41 Two protons are removed from sp^3 carbons to make sp^2 carbons and to generate a π system with 10 π electrons.



16-42

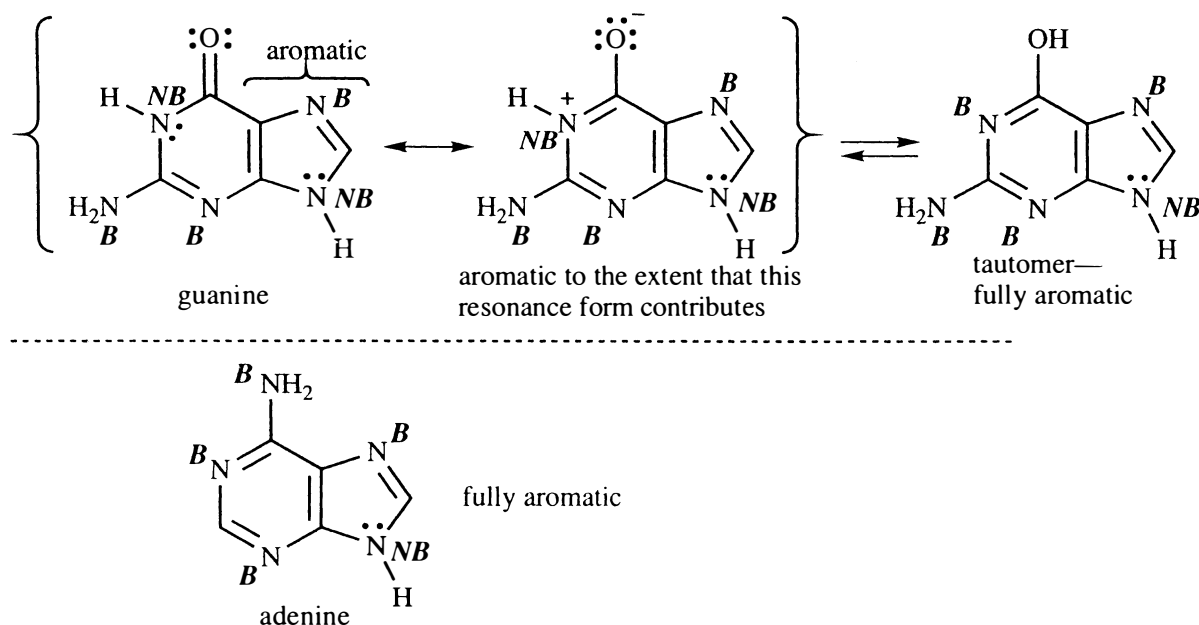


16-43 These four bases can be aromatic, partially aromatic, or aromatic in a tautomeric form. In other words, aromaticity plays an important role in the chemistry of all four structures. (Only electron pairs involved in the important resonance are shown.) For part (b), nitrogens that are basic are denoted by **B**. Those that are not basic are shown as **NB**. Note that some nitrogens change depending on the tautomeric form.



continued on the next page

16-43 continued

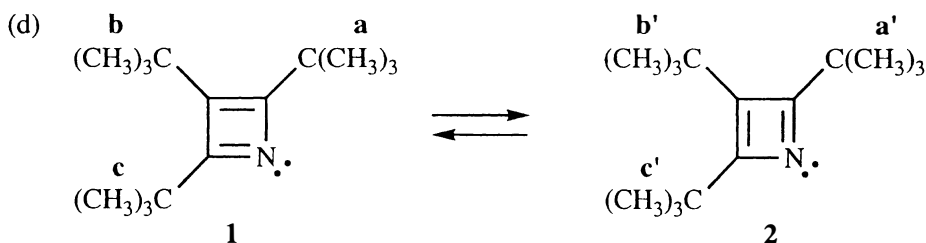


16-44

(a) Antiaromatic—only 4 π electrons.

(b) This molecule is electronically equivalent to cyclobutadiene. Cyclobutadiene is unstable and undergoes a Diels-Alder reaction with another molecule of itself. The *t*-butyl groups prevent dimerization by blocking approach of any other molecule.

(c) Yes, the nitrogen should be basic. The pair of electrons on the nitrogen is in an sp^2 orbital and is not part of the π system.



Analysis of structure **1** shows the three *t*-butyl groups in unique environments in relation to the nitrogen. We would expect three different signals in the NMR, as is observed at -110°C . Why do signals coalesce as the temperature is increased? Two of the *t*-butyl groups become equivalent—which two? Most likely, they are **a** and **c** that become equivalent as they are symmetric around the nitrogen. But they are *not* equivalent in structure **1**—what is happening here?

What must happen is an equilibration between structures **1** and **2**, very slow at -110°C , but very fast at room temperature, faster than the NMR can differentiate. So the signal which has coalesced is an average of **a** and **a'** and **c** and **c'**. (This type of low temperature NMR experiment is also used to differentiate axial and equatorial hydrogens on a cyclohexane.)

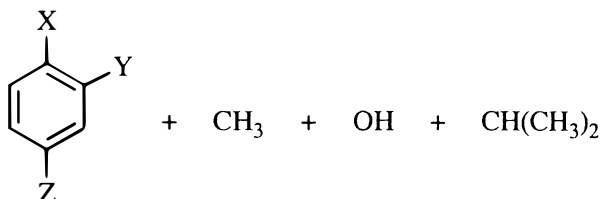
The NMR data prove that **1** is not aromatic, and that **1** and **2** are isomers, not resonance forms. If **1** were aromatic, then **a** and **c** would have identical NMR signals at all temperatures.

Mass spectrum: Molecular ion at 150; base peak at 135, $M - 15$, is loss of methyl.

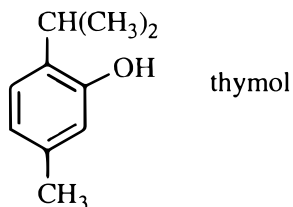
Infrared spectrum: The broad peak at 3500 cm^{-1} is OH; thymol must be an alcohol. The peak at 1620 cm^{-1} suggests an aromatic compound.

NMR spectrum: The singlet at δ 4.8 is OH; it disappears upon shaking with D_2O . The 6H doublet at δ 1.2 and the 1H multiplet at δ 3.2 are an isopropyl group, apparently on the benzene ring. A 3H singlet at δ 2.3 is a methyl group, also on the benzene ring.

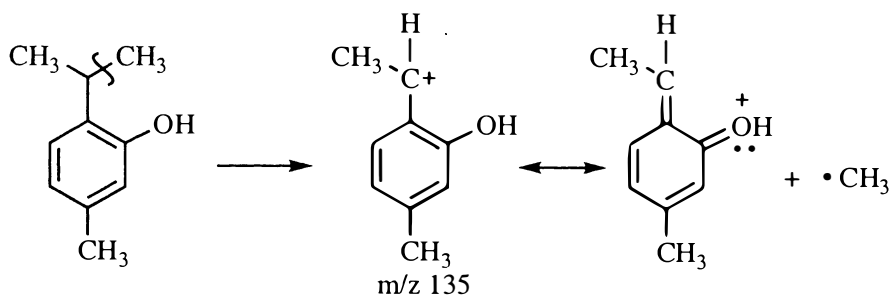
Analysis of the aromatic protons suggests the substitution pattern. The three aromatic hydrogens confirm that there are three substituents. The singlet at δ 6.5 is a proton between two substituents (no neighboring H's). The doublets at δ 6.75 and δ 7.1 are ortho hydrogens, splitting each other.



Several isomeric combinations are consistent with the spectra (although the single H giving δ 6.5 suggests that either Y or Z is the OH group—an OH on a benzene ring shields hydrogens ortho to it, moving them upfield). The structure of thymol is:



The final question is how the molecule fragments in the mass spectrometer:



resonance stabilization of this benzylic cation includes forms with positive charge on three ring carbons and on oxygen (shown)

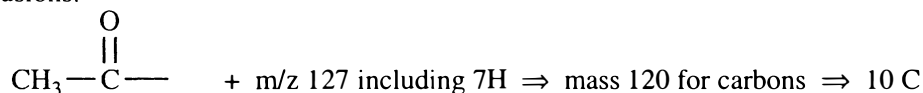
16-46

Mass spectrum: Molecular ion at 170; two prominent peaks are $M - 15$ (loss of methyl) and $M - 43$ (as we shall see, most likely the loss of acetyl, CH_3CO).

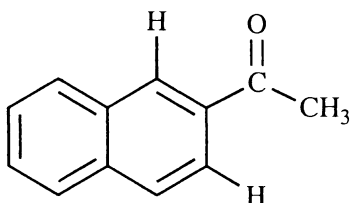
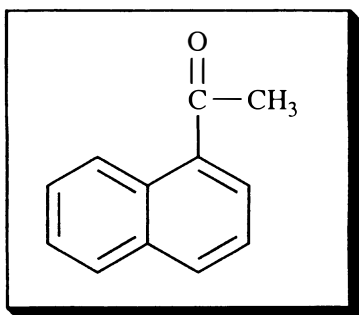
Infrared spectrum: The two most significant peaks are at 1680 cm^{-1} (conjugated carbonyl) and 1600 cm^{-1} (aromatic $\text{C}=\text{C}$).

NMR spectrum: A 3H singlet at δ 2.7 is methyl next to a carbonyl, shifted slightly downfield by an aromatic ring. The other signals are seven aromatic protons. The 1H at d 8.7 is a deshielded proton next to a carbonyl. Since there is only one, the carbonyl can have only one neighboring hydrogen.

Conclusions:



The fragment C_{10}H_7 is almost certainly a naphthalene. The correct isomer (box) is indicated by the NMR.

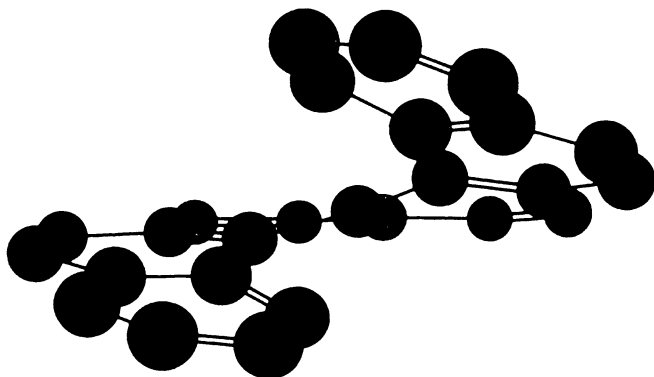


This isomer would have two deshielded protons in the NMR.

16-47

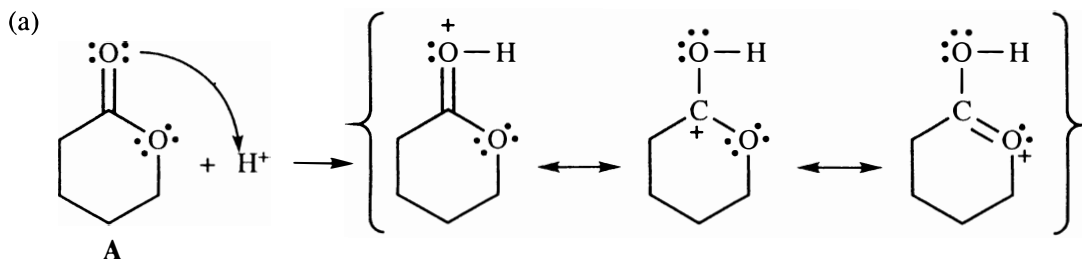
Although all carbons in hexahelicene are sp^2 , the molecule is not flat. Because of the curvature of the ring system, one end of the molecule has to sit on top of the other end—the carbons and the hydrogens would bump into each other if they tried to occupy the same plane. In other words, the molecule is the beginning of a spiral. An "upward" spiral is the nonsuperimposable mirror image of a "downward" spiral, so the molecule is chiral and therefore optically active.

The magnitude of the optical rotation is extraordinary: it is one of the largest rotations ever recorded. In general, alkanes have small rotations and aromatic compounds have large rotations, so it is reasonable to expect that it is the interaction of plane-polarized light (electromagnetic radiation) with the electrons in the twisted pi system (which can also be considered as having wave properties) that causes this enormous rotation.

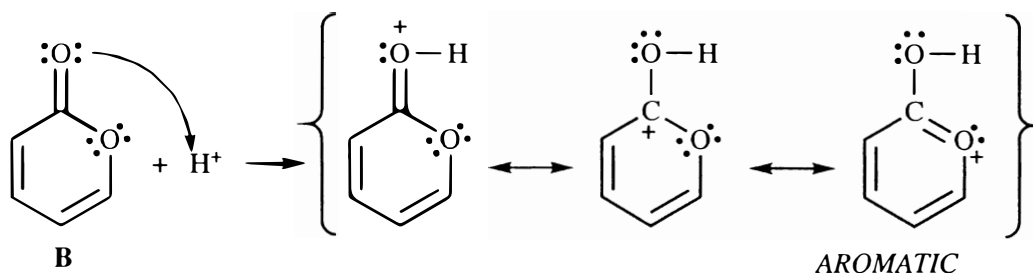


three-dimensional picture of hexahelicene showing the twist in the system of six rings

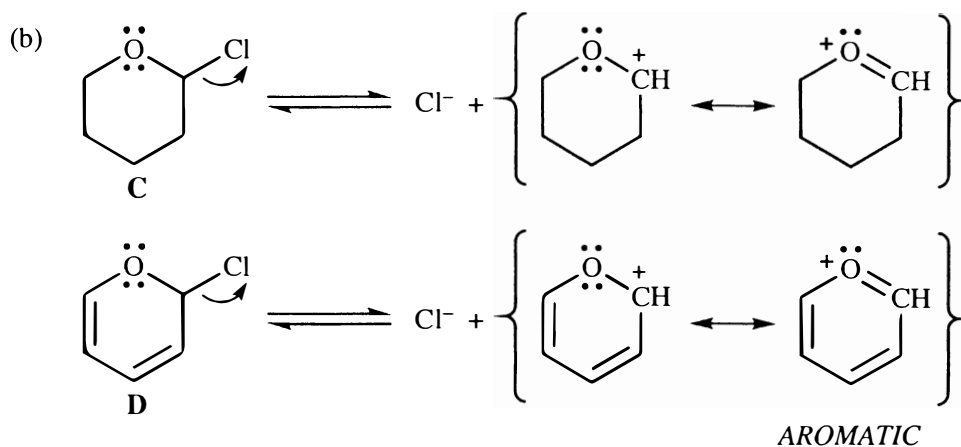
16-48 The key concept in parts (a)-(c) is that an aromatic product is created.



The protonated carbonyl gives a resonance-stabilized cation. Protonation of the singly bonded oxygen does not generate a resonance-stabilized product.



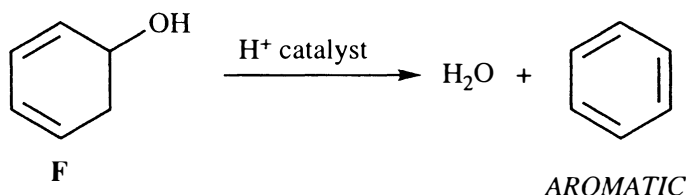
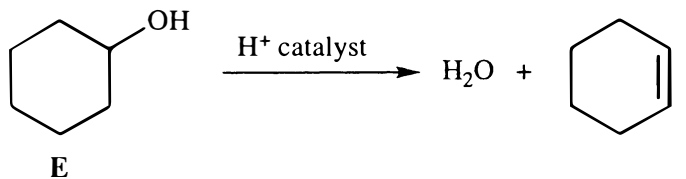
The last resonance form shows that the cation produced is aromatic and therefore more stable than the corresponding nonaromatic ion. In this second reaction, the products are more favored than in the first reaction which is interpreted as the reactant **B** being more basic than **A**.



The product from ionization of **C** is stabilized by resonance. The ionization product of **D** is not only resonance-stabilized but is also aromatic and therefore more stable. A reaction that produces a more stable product will usually happen faster under milder conditions because the transition state leading to that product will be stabilized, leading to a lower activation energy.

16-48 continued

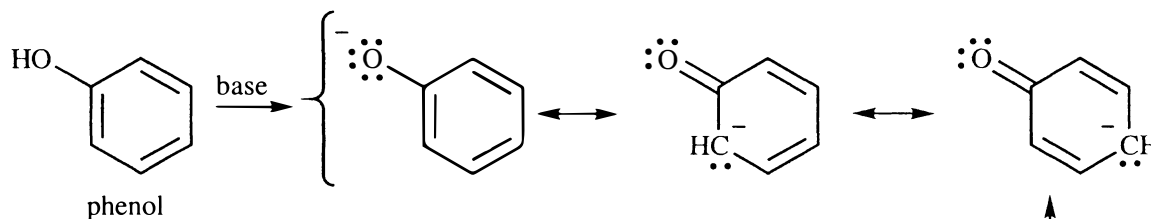
(c)



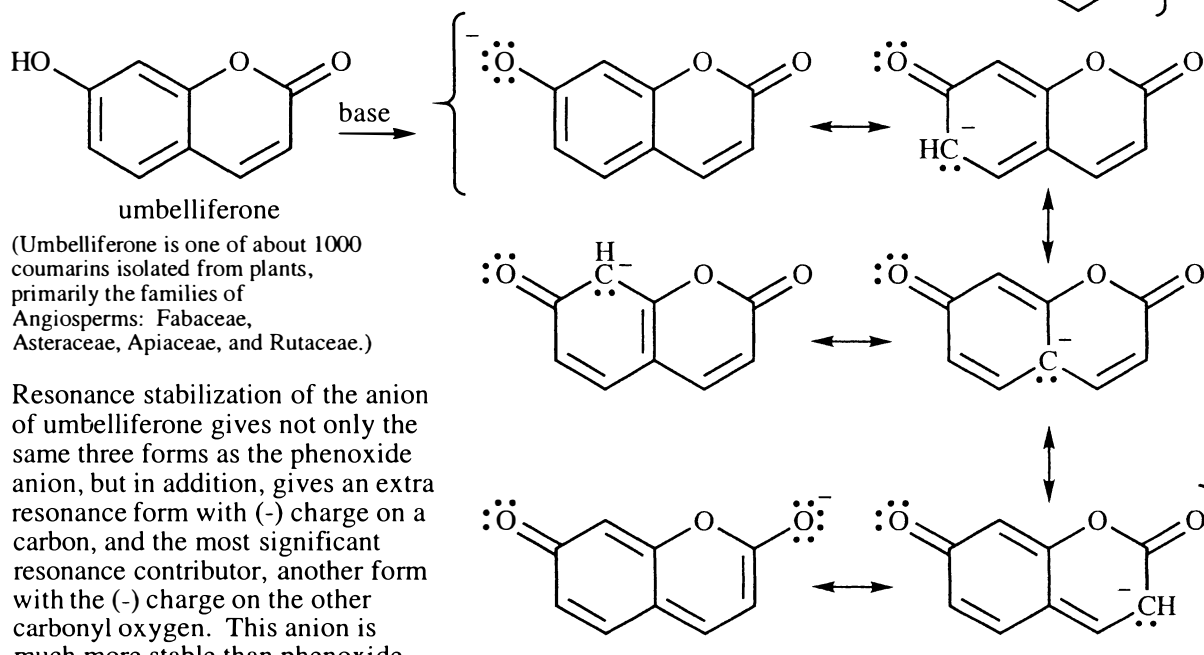
Dehydration of **F** produces an aromatic product that is more stable than the product from **E**. A reaction that produces a more stable product will usually happen faster under milder conditions because the transition state leading to that product will be stabilized, leading to a lower activation energy.

AROMATIC

(d)



Resonance stabilization of the phenoxide anion shows the negative charge distributed over the one para and two ortho carbons.

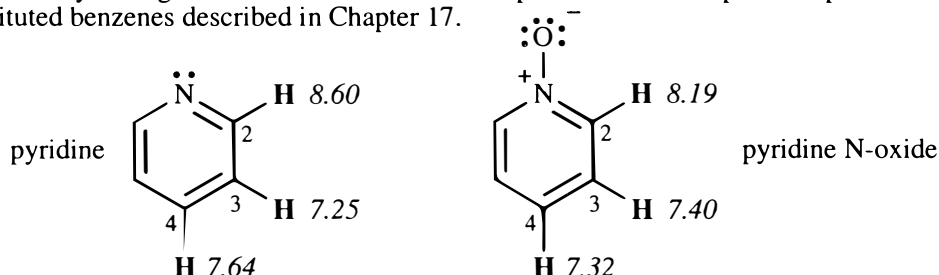


(Umbelliferone is one of about 1000 coumarins isolated from plants, primarily the families of Angiosperms: Fabaceae, Asteraceae, Apiaceae, and Rutaceae.)

Resonance stabilization of the anion of umbelliferone gives not only the same three forms as the phenoxide anion, but in addition, gives an extra resonance form with (-) charge on a carbon, and the most significant resonance contributor, another form with the (-) charge on the other carbonyl oxygen. This anion is much more stable than phenoxide which we interpret as enhanced acidity of the starting material, umbelliferone. In fact, the pK_a of umbelliferone is 7.7 while phenol is about 10.

16-49 Humulon (sometimes spelled humulone), even though highly resonance stabilized, cannot be aromatic because the carbon shown at the bottom of the ring is tetrahedral and must be sp^3 hybridized. A ring is aromatic only when all of the atoms in the ring have a p orbital which the sp^3 carbon does not.

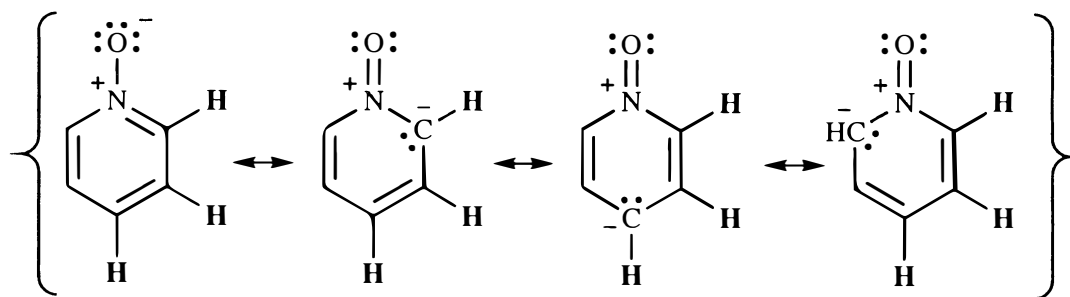
16-50 Are you familiar with the concept "tough love", that is, sometimes you have to be stern with someone you love for their own good? The concept is that sometimes to demonstrate one emotion, the behavior has to appear exactly the opposite. Granted, this is a stretch to apply it to atoms, but the point is that sometimes atoms like oxygen and nitrogen can have conflicting effects: they can withdraw electron density by their strong electronegativity (an inductive effect) but at the same time, they can donate electron density through their resonance effect. This phenomenon will prove important in the reactivity of substituted benzenes described in Chapter 17.



Nitrogen is electronegative, so it exerts a deshielding effect on H-2 in pyridine. The effect diminishes with distance as expected with an inductive effect, although it is harder to explain why H-4 is deshielded more than H-3.

In pyridine N-oxide, with an even more electronegative oxygen attached to the N, it would be reasonable to expect that the hydrogens would be deshielded. This is the case with H-3; we can infer that the effect on H-3 is purely an inductive effect.

Even more interesting is the *shielding* effect on H-2 and H-4; these chemical shifts are shifted *upfield*. This must reflect the other side of oxygen's personality, the donation of electron density through a resonance effect. Drawing the resonance forms clearly shows that the electron density at H-2 and H-4 (and presumably H-6) increases through this donation by resonance, in perfect agreement with the NMR results. As we will see in Chapter 17, in most cases, resonance effect trumps inductive effect.



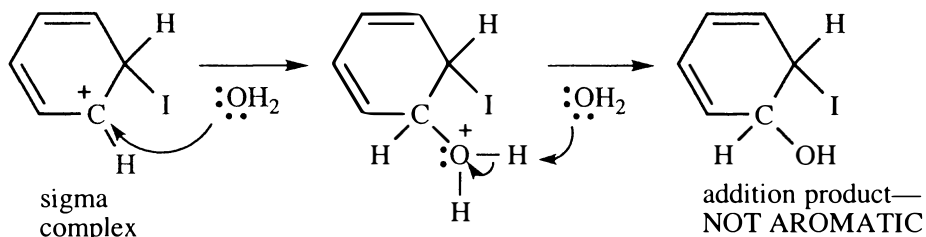
Note: The practice of applying human emotions to inanimate objects is called "anthropomorphizing". For example, we say that an atom is "happy" when it has a full octet of electrons. In casual conversation, this gets a point across, but it is not appropriate in rigorous scientific terms, for example, on exams. Under more formal conditions, we are expected to use the specific terms of science because they are well defined and do not permit sloppy or fuzzy concepts.

As our equipment technician says: "Don't anthropomorphize computers. They hate that."

CHAPTER 17—REACTIONS OF AROMATIC COMPOUNDS

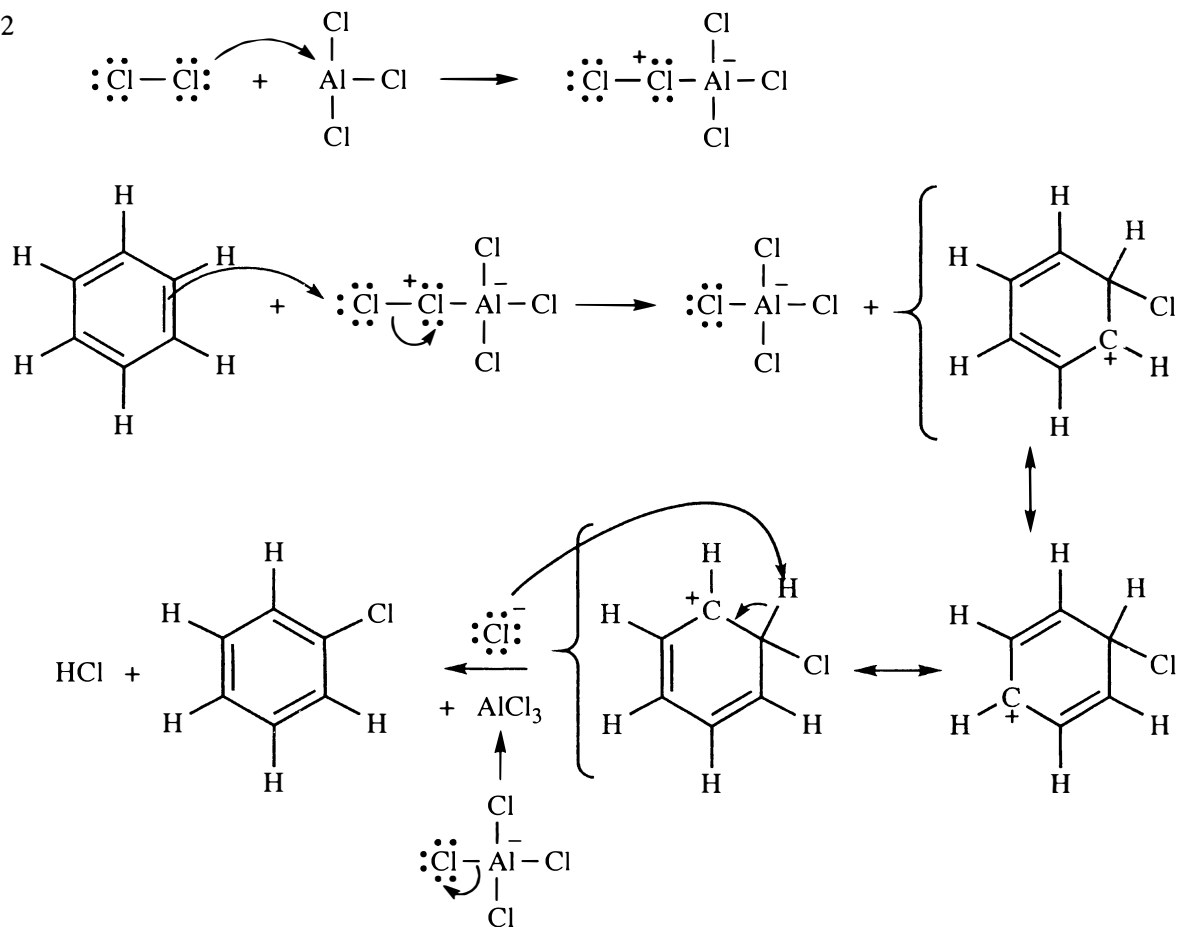
The representation of benzene with a circle to represent the π system is fine for questions of nomenclature, properties, isomers, and reactions. For questions of mechanism or reactivity, however, the representation with three alternating double bonds (the Kekulé picture) is more informative. For clarity and consistency, this Solutions Manual will use the Kekulé form exclusively.

17-1

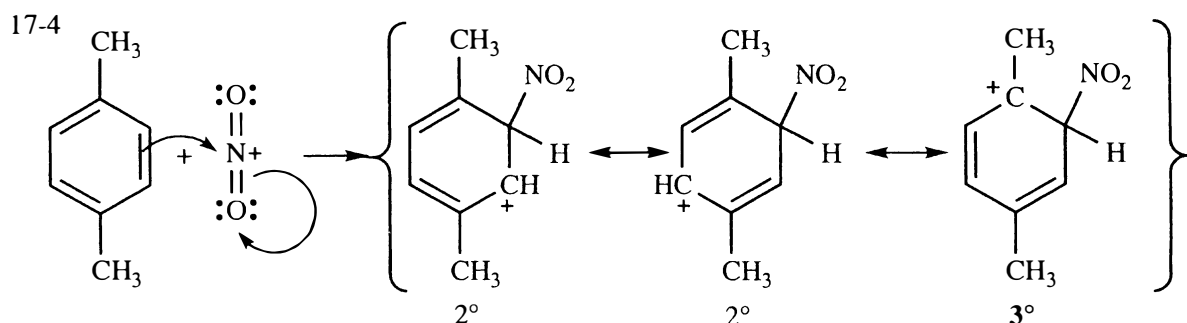
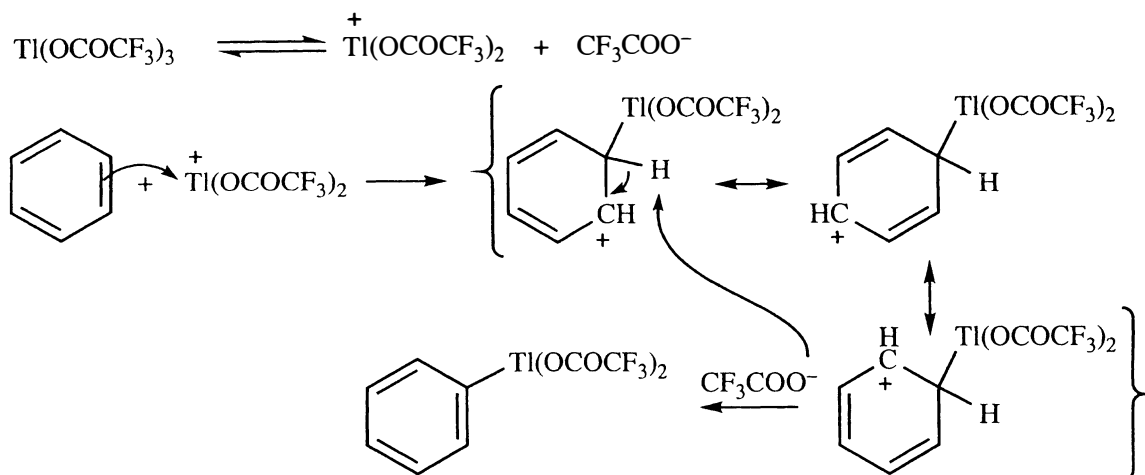


While the addition of water to the sigma complex can be shown in a reasonable mechanism, the product is not aromatic. Thus, it has lost the 152 kJ/mol (36 kcal/mole) of resonance stabilization energy. The addition reaction is not favorable energetically, and substitution prevails.

17-2

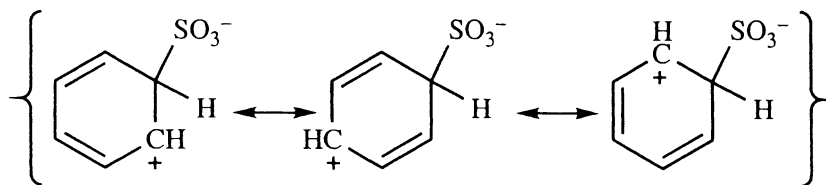


17-3 Like most heavy metals, thallium is highly toxic and should not be used on breakfast cereal.

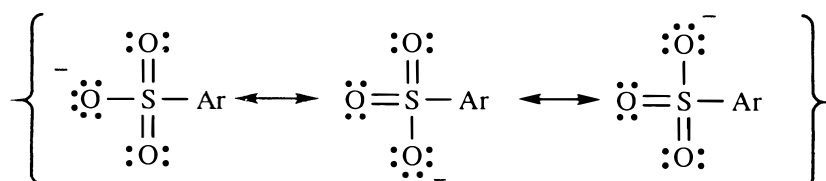


Benzene's sigma complex has positive charge on three 2° carbons. The sigma complex above shows positive charge in one resonance form on a 3° carbon, lending greater stabilization to this sigma complex. The more stable the intermediate, the lower the activation energy required to reach it, and the faster the reaction will be.

17-5 delocalization of the positive charge on the ring



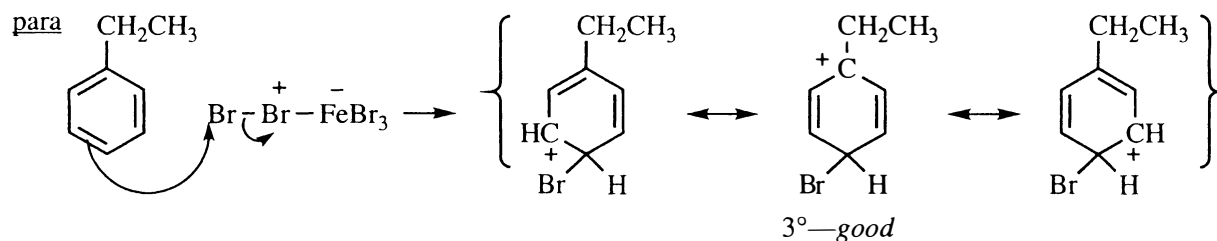
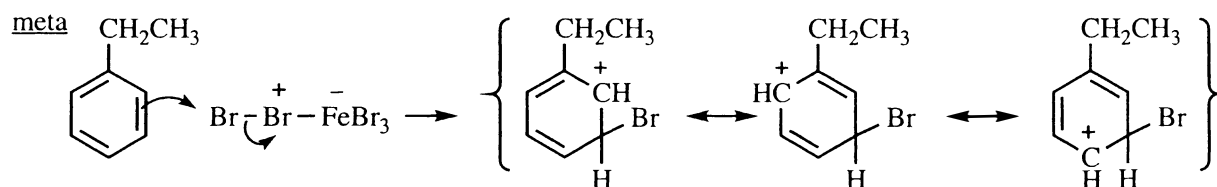
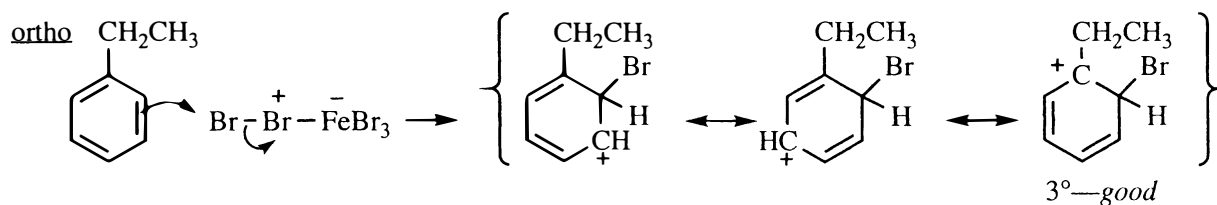
delocalization of the negative charge on the sulfonate group



("Ar" is the general abbreviation for an "aromatic" or "aryl" group, in this case, benzene; "R" is the general abbreviation for an "aliphatic" or "alkyl" group.)

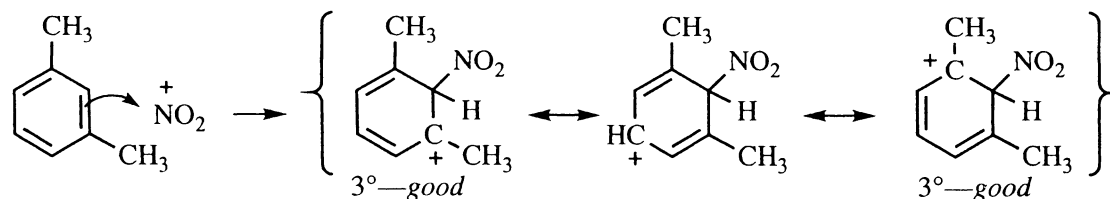
17-6

(a) The key to electrophilic aromatic substitution lies in the stability of the sigma complex. When the electrophile bonds at ortho or para positions of ethylbenzene, the positive charge is shared by the 3° carbon with the ethyl group. Bonding of the electrophile at the meta position lends no particular advantage because the positive charge in the sigma complex is never adjacent to, and therefore never stabilized by, the ethyl group.

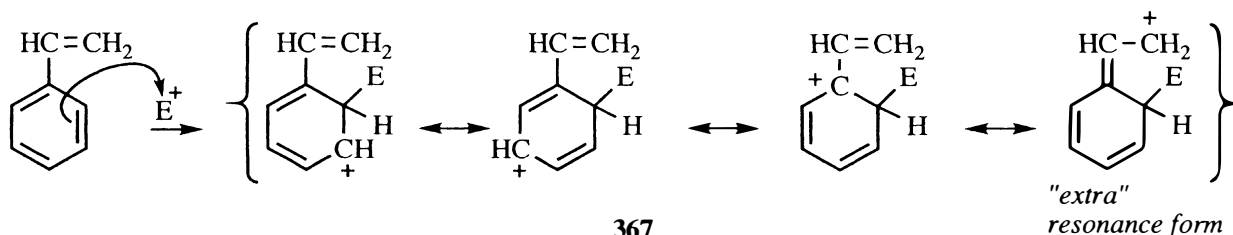


(b) Electrophilic attack on *p*-xylene gives an intermediate in which only one of the three resonance forms is stabilized by a substituent (see the solution to Problem 17-4). *m*-Xylene, however, is stabilized in two of its three resonance forms. A more stable intermediate gives a faster reaction.

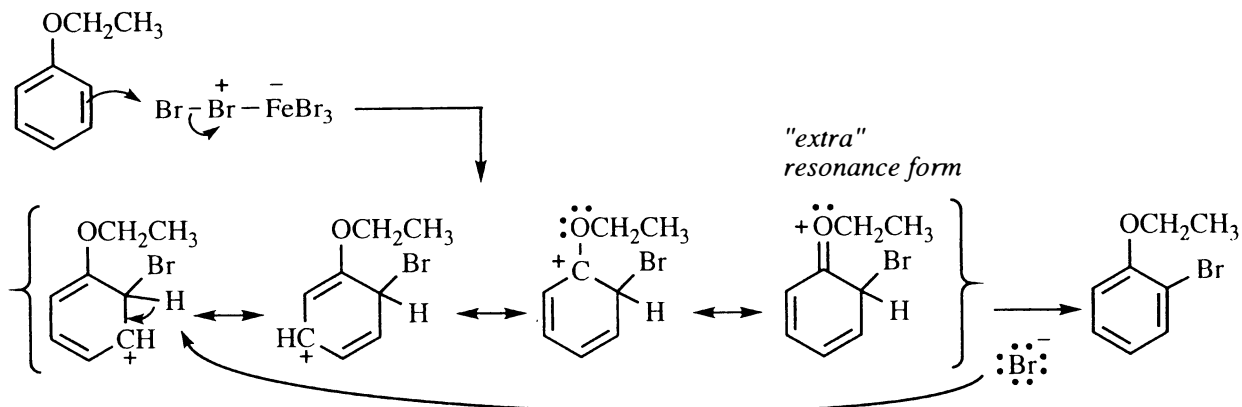
m-xylene



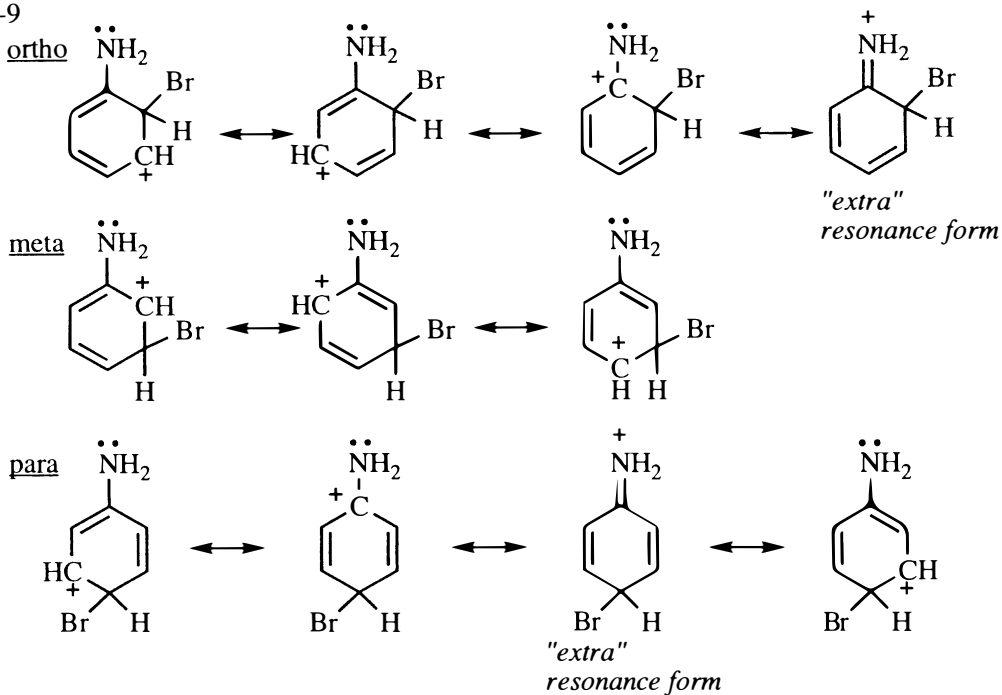
17-7 For ortho and para attack, the positive charge in the sigma complex can be shared by resonance with the vinyl group. This cannot happen with meta attack because the positive charge is never adjacent to the vinyl group. (Ortho attack is shown; para attack gives an intermediate with positive charge on the same carbons.)



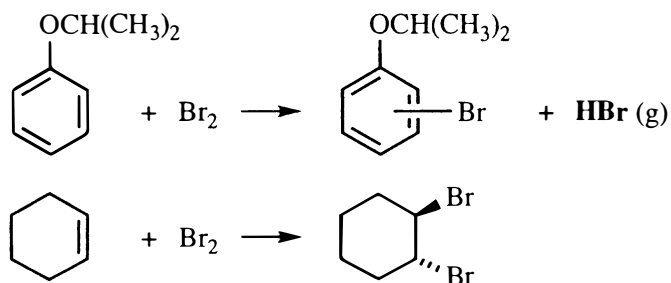
17-8 Attack at only ortho and para positions (not meta) places the positive charge on the carbon with the ethoxy group, where the ethoxy group can stabilize the positive charge by resonance donation of a lone pair of electrons. (Ortho attack is shown; para attack gives a similar intermediate.)



17-9



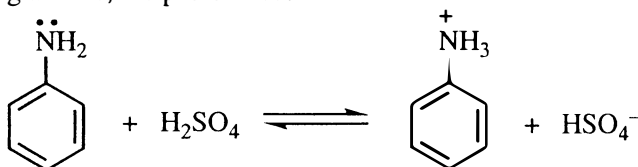
17-10



Substitution generates HBr whereas the addition does not. If the reaction is performed in an organic solvent, bubbles of HBr can be observed, and HBr gas escaping into moist air will generate a cloud. If the reaction is performed in water, then adding moist litmus paper to test for acid will differentiate the results of the two compounds.

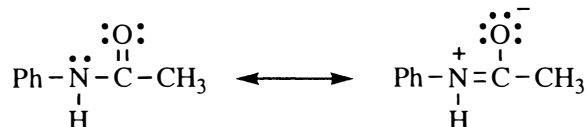
17-11

(a) Nitration is performed with nitric acid and a sulfuric acid catalyst. In strong acid, amines in general, including aniline, are protonated.



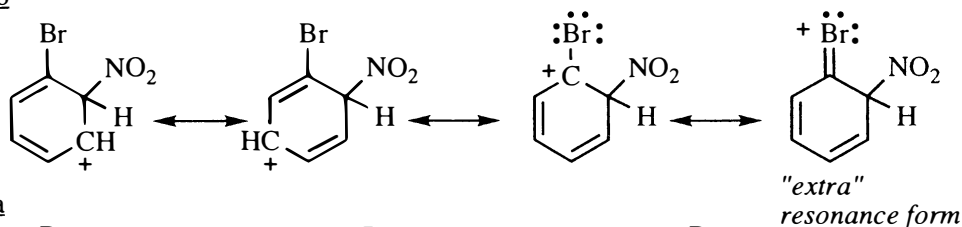
(b) The NH_2 group is a strongly activating ortho,para-director. In acid, however, it exists as the protonated ammonium ion—a strongly **deactivating meta-director**. The strongly acidic nitrating mixture itself forces the reaction to be slower.

(c) The acetyl group removes some of the electron density from the nitrogen, making it much less basic; the nitrogen of this amide is not protonated under the reaction conditions. The N retains enough electron density to share with the benzene ring, so the NHCOCH_3 group is still an activating ortho,para-director, though weaker than NH_2 .

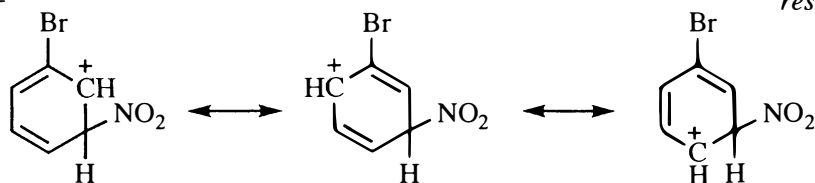


17-12 Nitronium ion attack at the ortho and para positions places positive charge on the carbon adjacent to the bromine, allowing resonance stabilization by an unshared electron pair from the bromine. Meta attack does not give a stabilized intermediate.

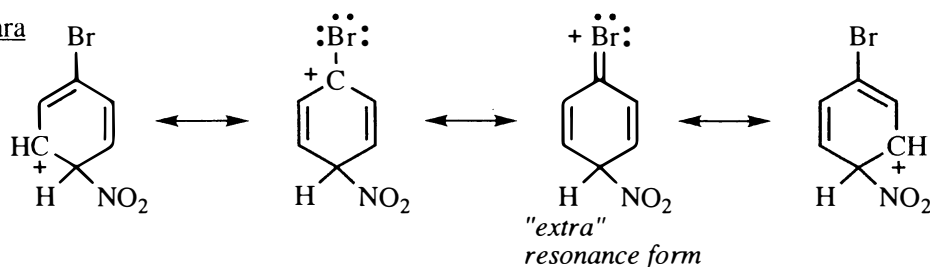
ortho



meta

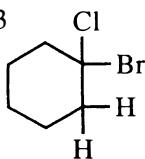


para

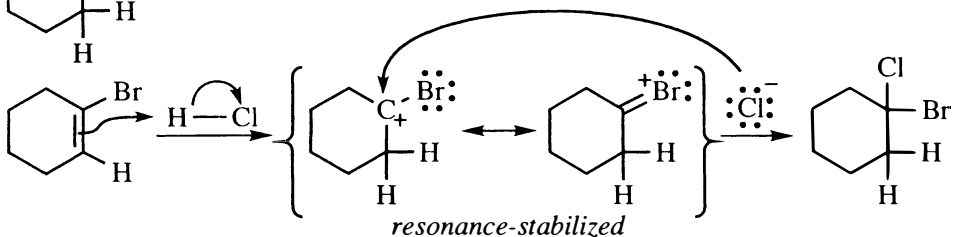


17-13

(a)



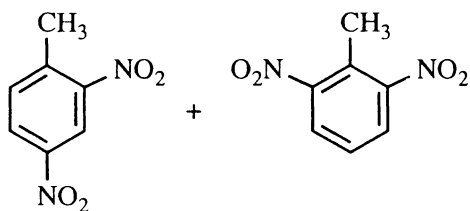
(b)



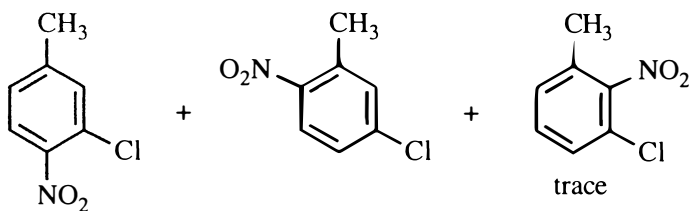
(c) A bromine atom can stabilize positive charge by sharing a pair of electrons. Bromine can do this in any cationic species, whether from electrophilic addition or electrophilic aromatic substitution.

17-14

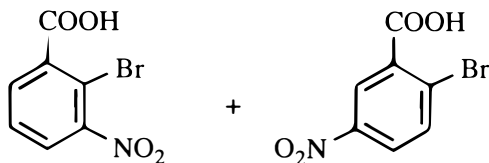
(a)



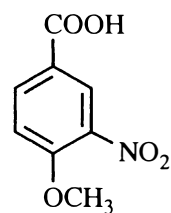
(b)



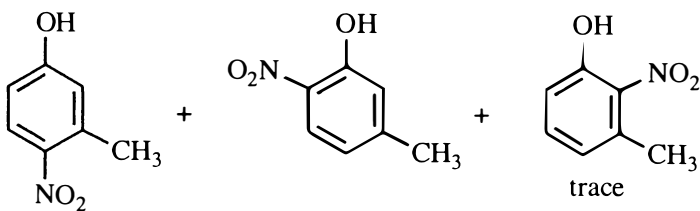
(c)



(d)

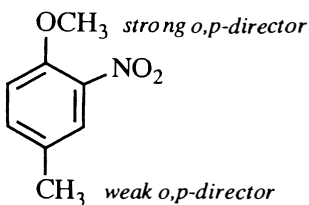


(e)

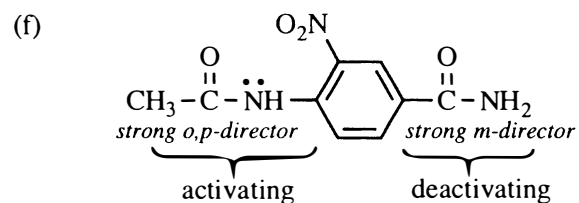
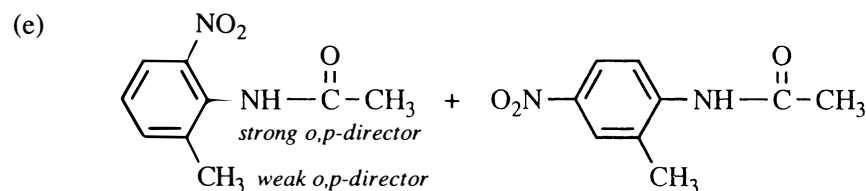
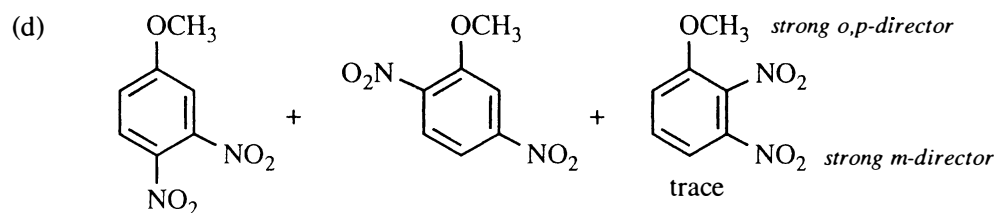
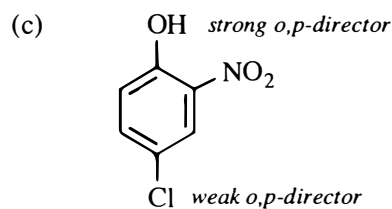
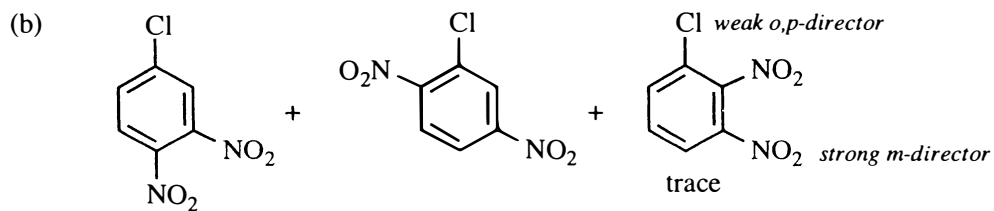


17-15

(a)

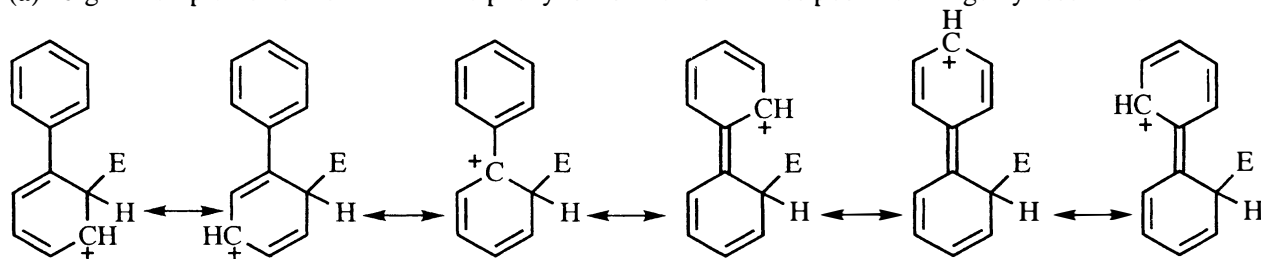


17-15 continued



17-16

(a) Sigma complex of ortho attack—the phenyl substituent stabilizes positive charge by resonance:

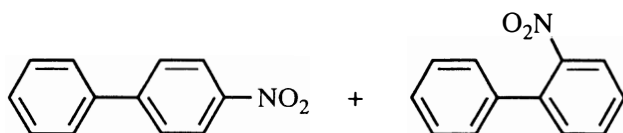


Para attack gives similar stabilization. Meta attack does not permit delocalization of the positive charge on the phenyl substituent.

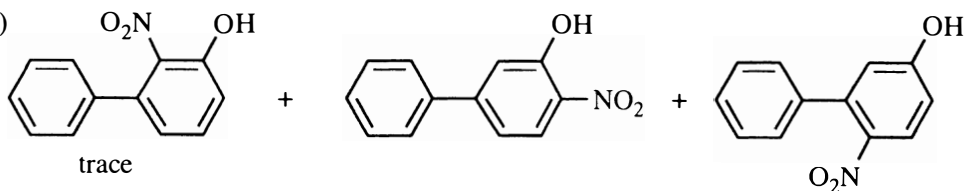
17-16 continued

(b)

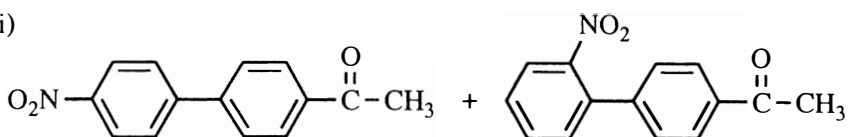
(i)



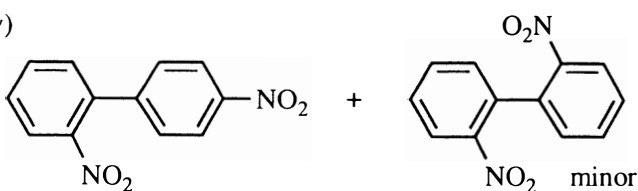
(ii)



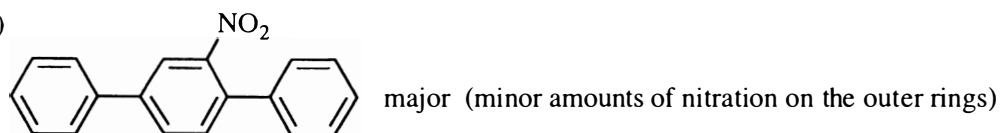
(iii)



(iv)

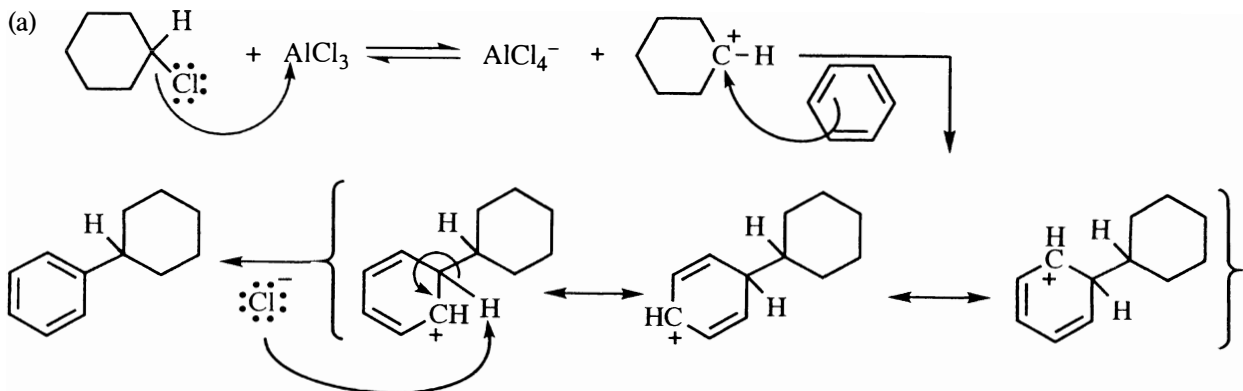


(v)



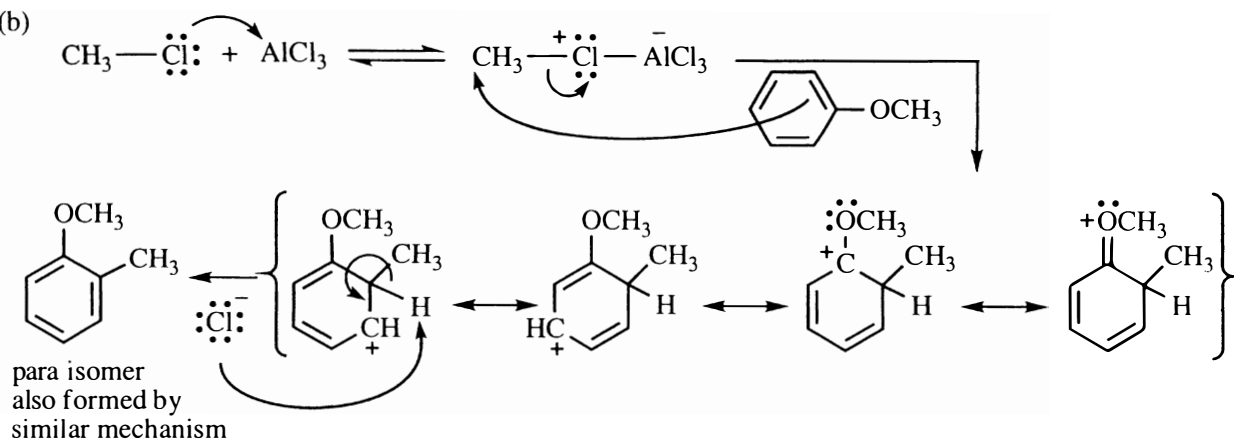
17-17

(a)

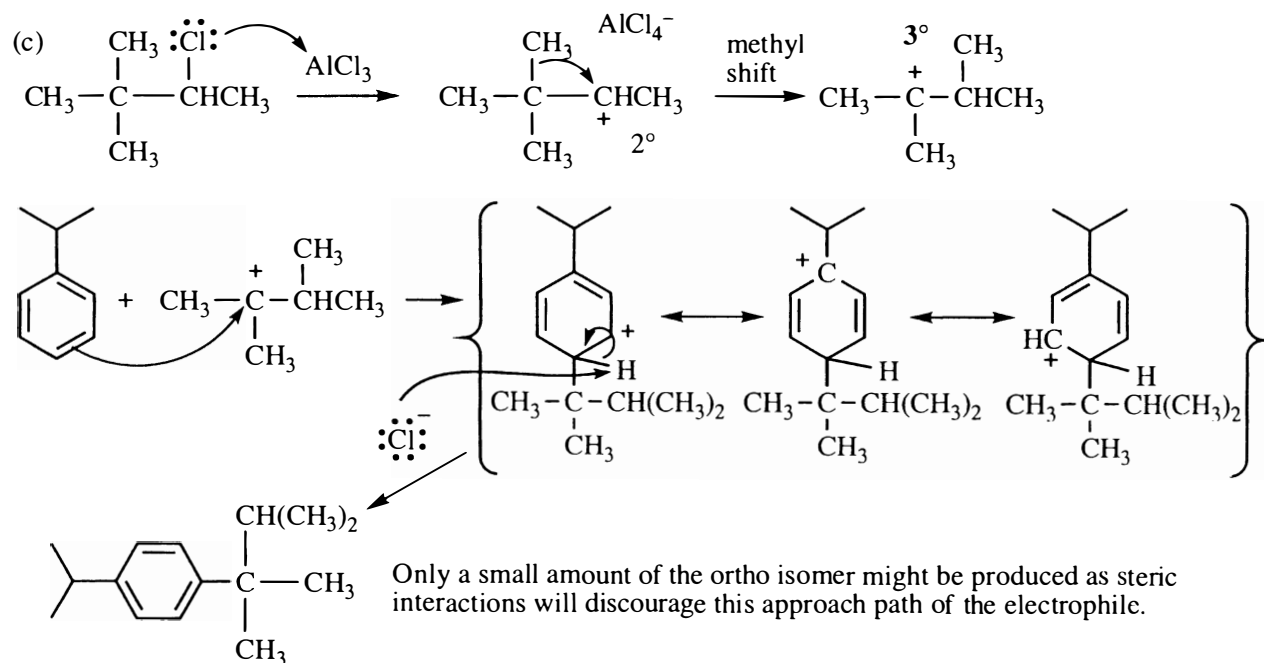


17-17 continued

(b)

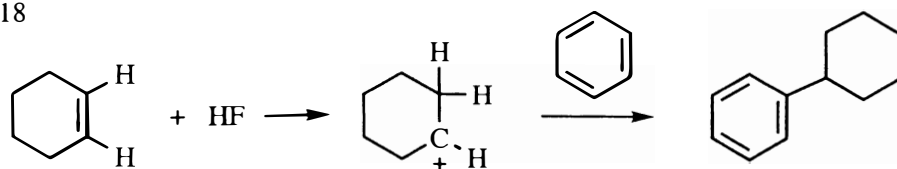


(c)

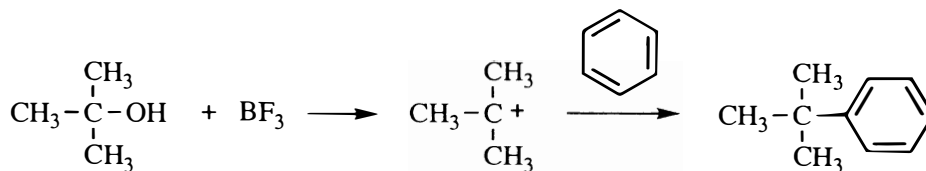


17-18

(a)

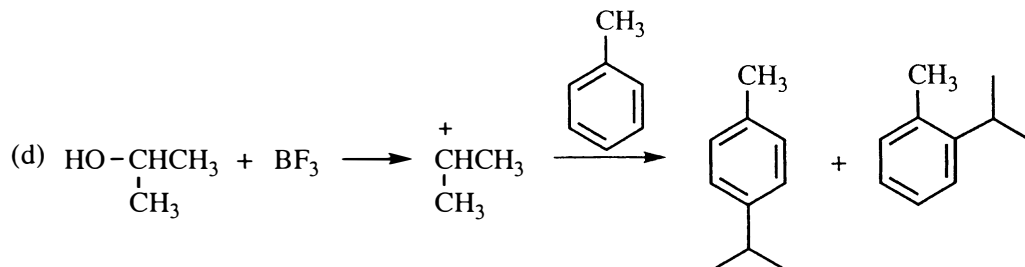
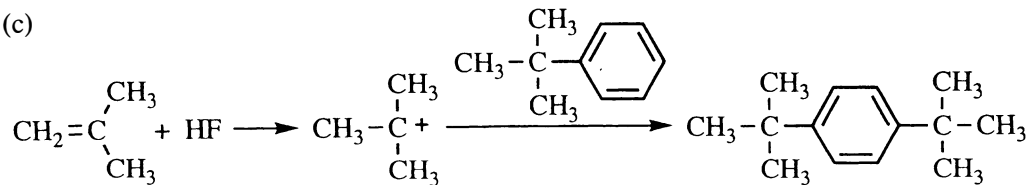


(b)

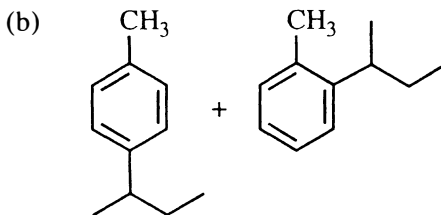
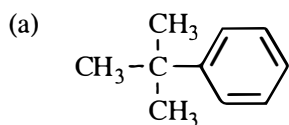


17-18 continued

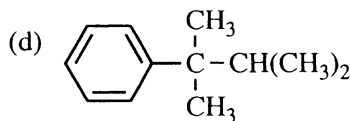
(c)



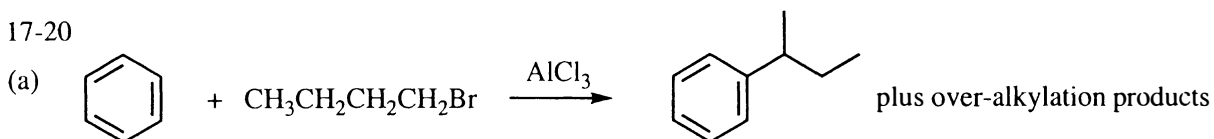
17-19 In (a), (b), and (d), the electrophile has rearranged.



(c) No reaction: nitrobenzene is too deactivated for the Friedel-Crafts reaction to succeed.



17-20



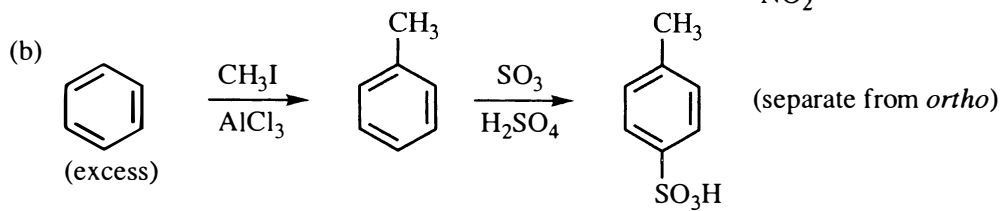
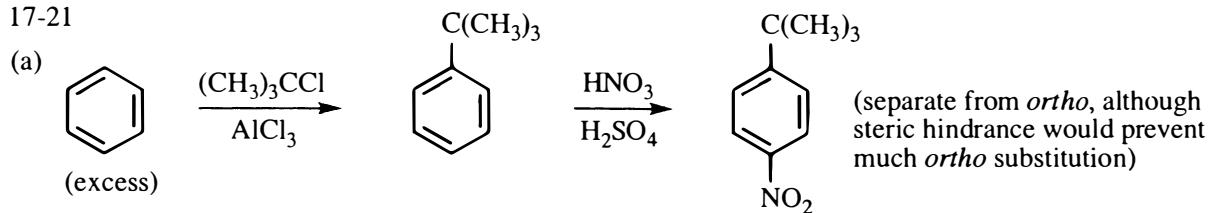
(b) gives desired product

(c) gives desired product, plus *ortho* isomer; use excess bromobenzene to avoid overalkylation

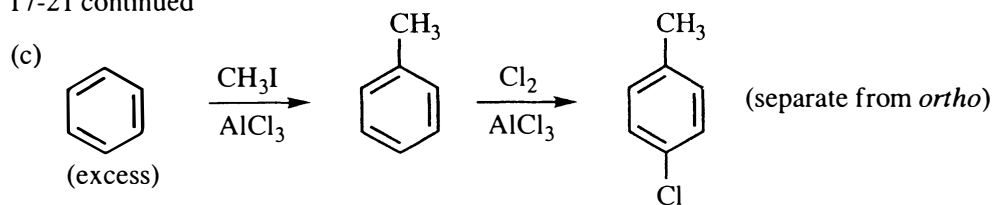
(d) gives desired product, plus *ortho* isomer

(e) gives desired product

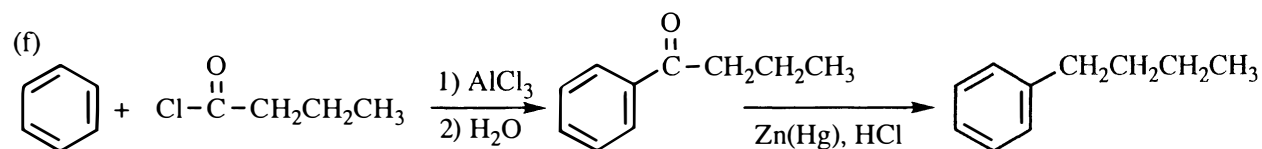
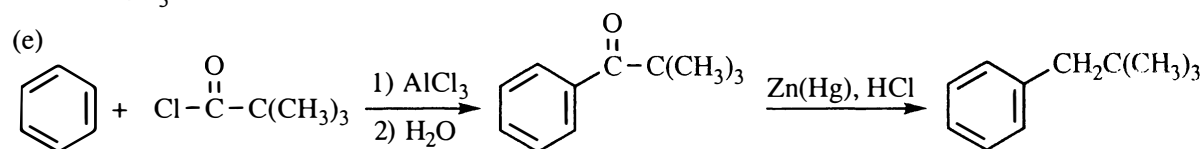
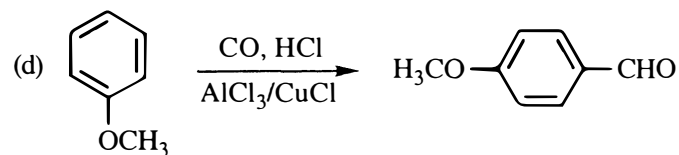
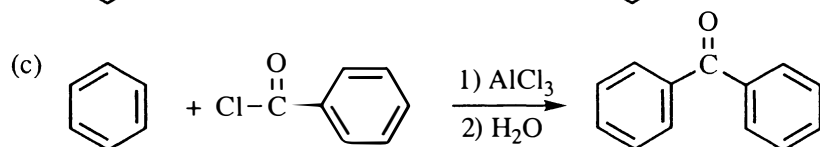
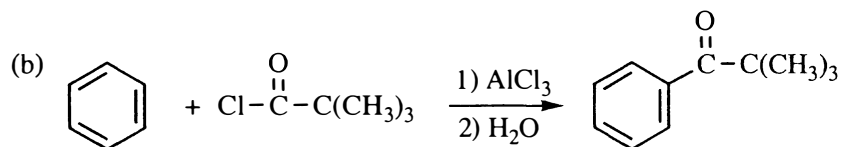
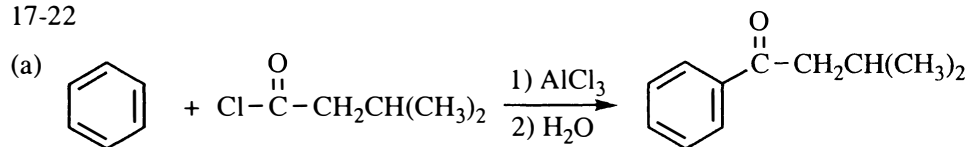
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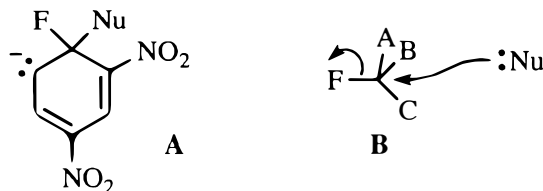
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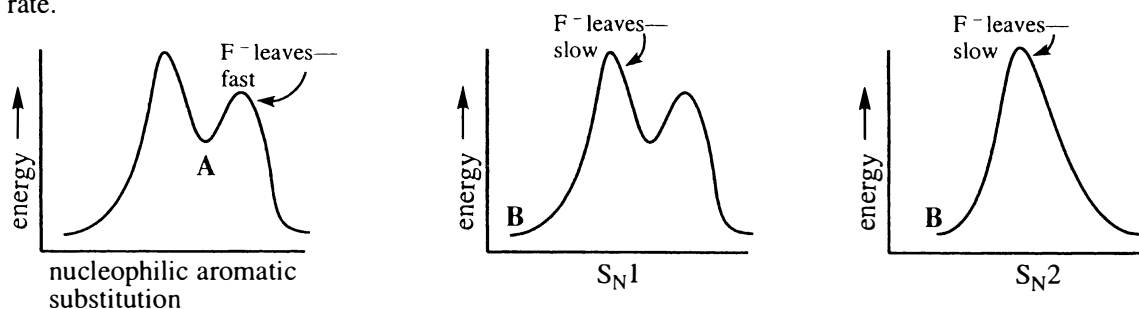
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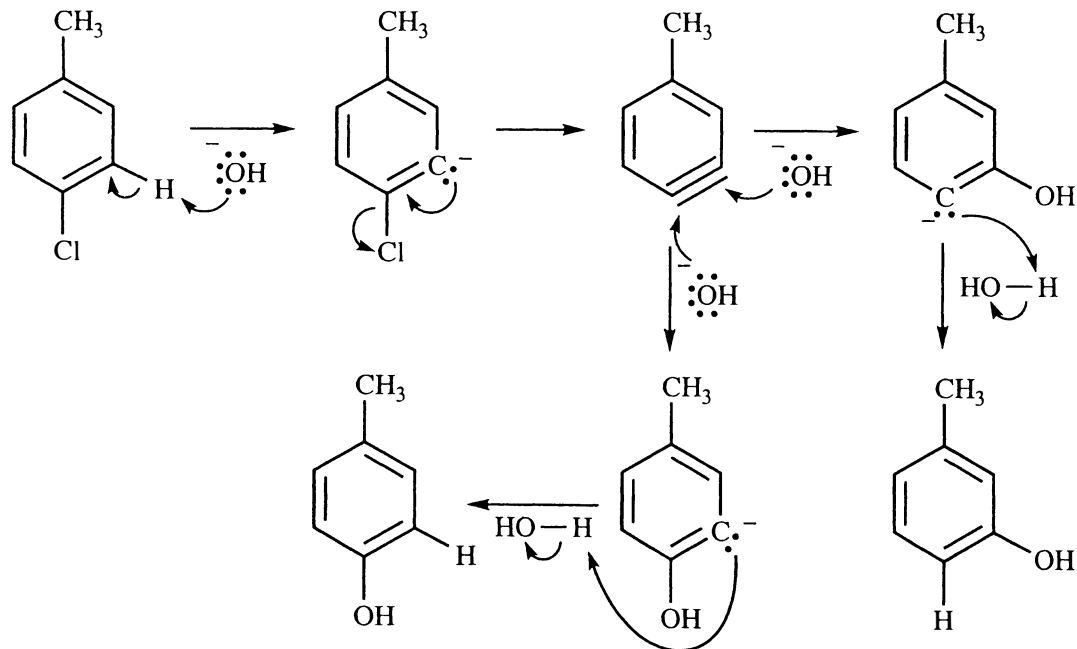
17-23 Another way of asking this question is this: Why is fluoride ion a good leaving group from **A** but not from **B** (either by S_N1 or S_N2)?



Formation of the anionic sigma complex **A** is the rate-determining (slow) step in nucleophilic aromatic substitution. The loss of fluoride ion occurs in a subsequent fast step where the nature of the leaving group does not affect the overall reaction rate. In the S_N1 or S_N2 mechanisms, however, the carbon-fluorine bond is breaking in the rate-determining step, so the poor leaving group ability of fluoride does indeed affect the rate.

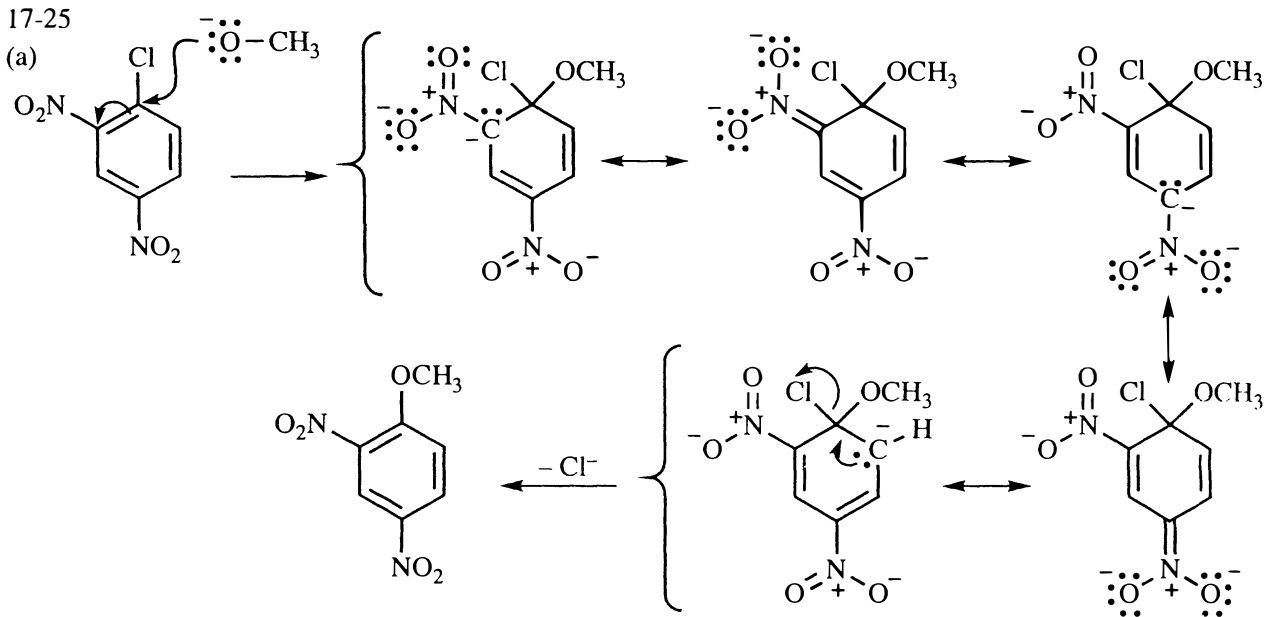


17-24

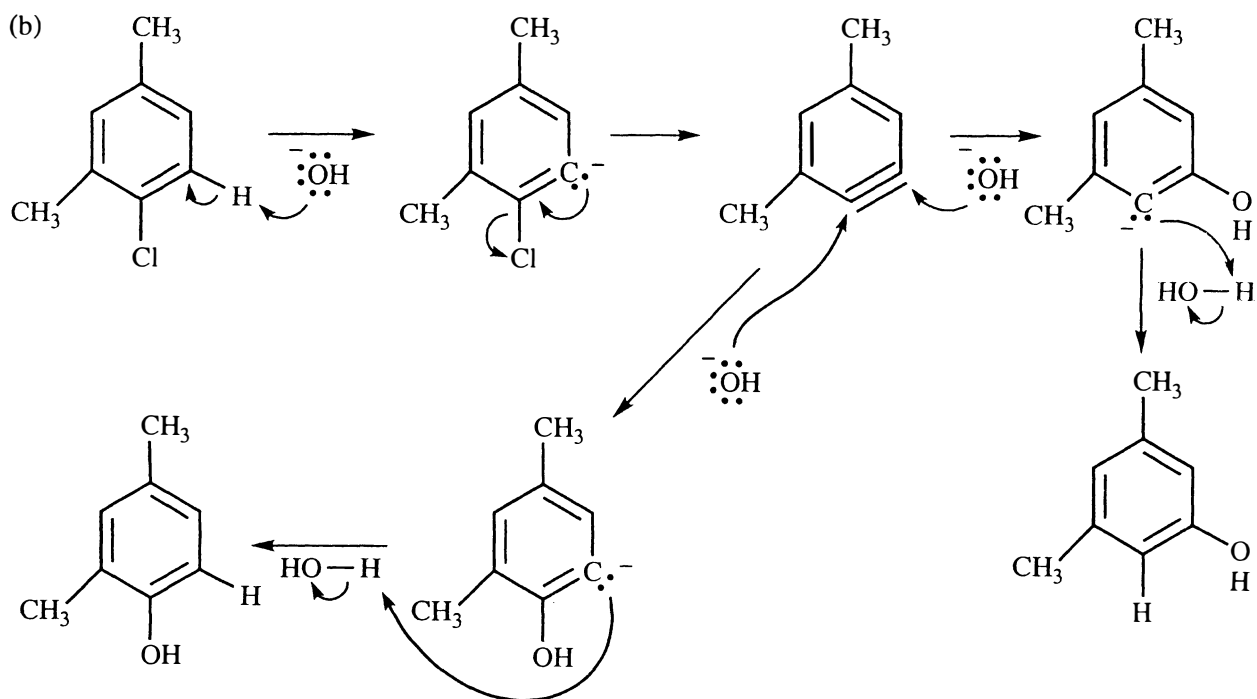


17-25

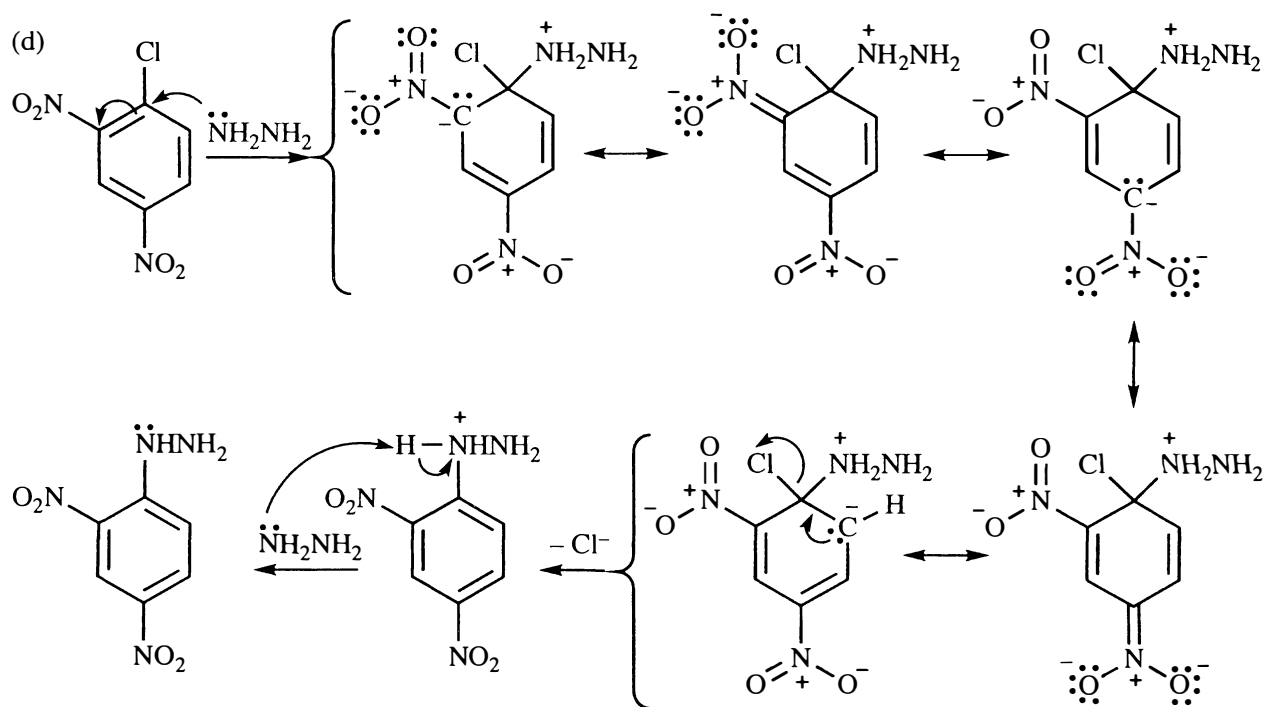
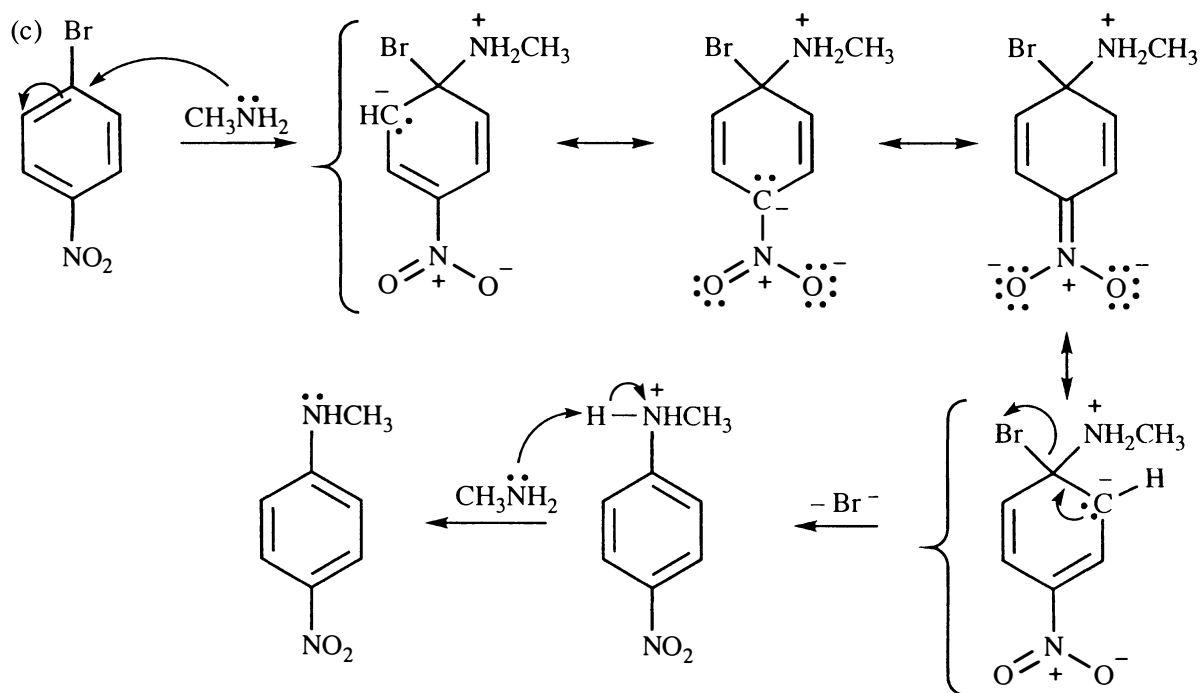
(a)



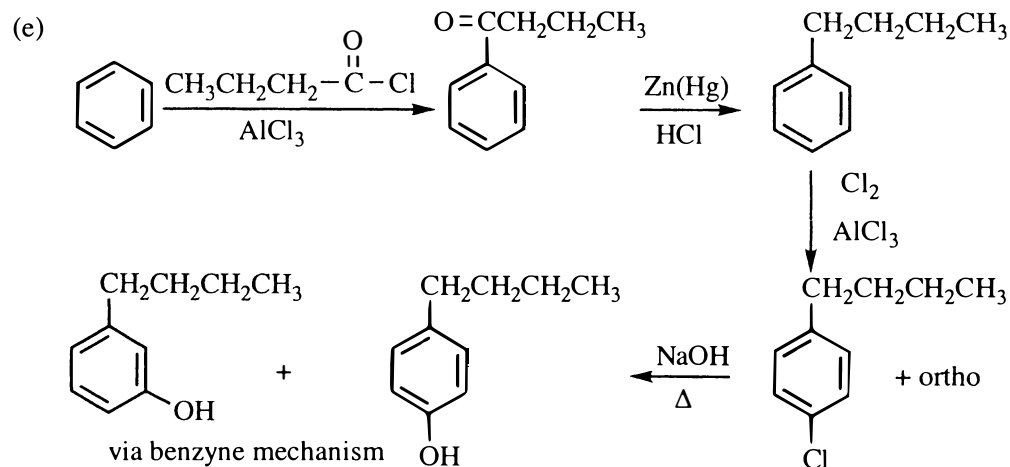
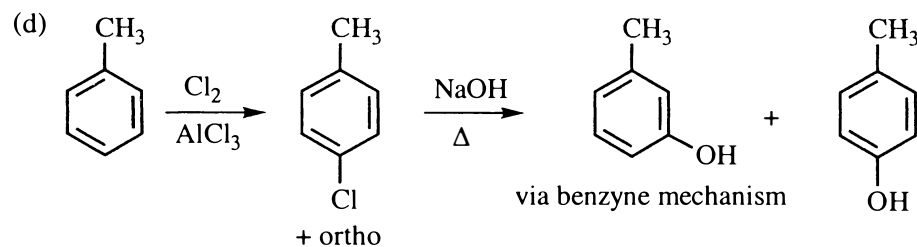
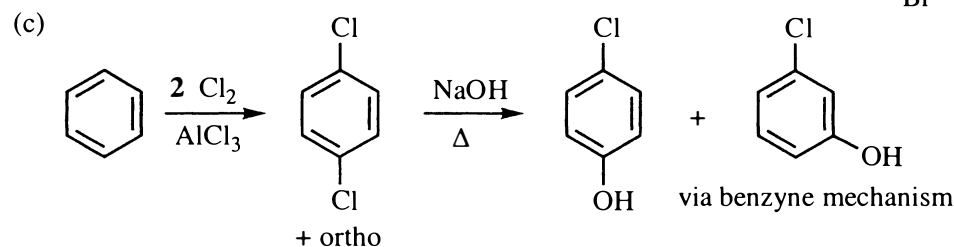
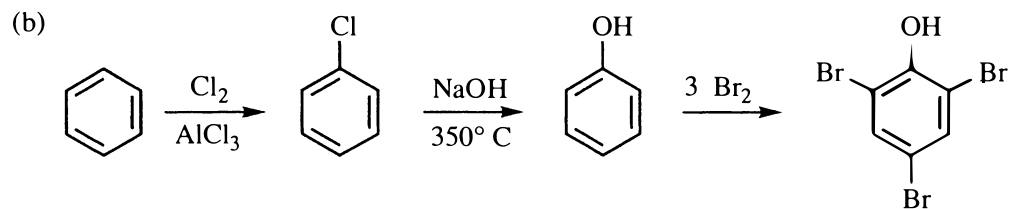
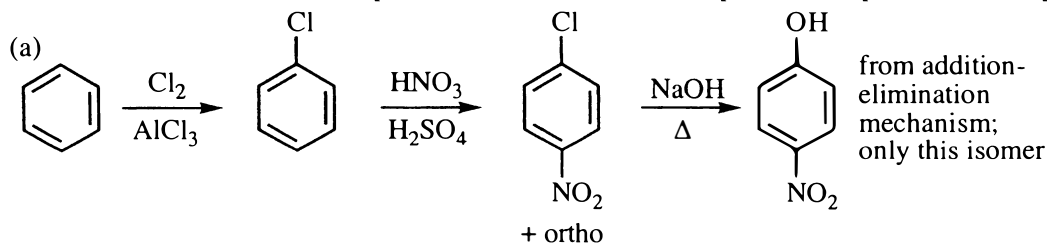
(b)



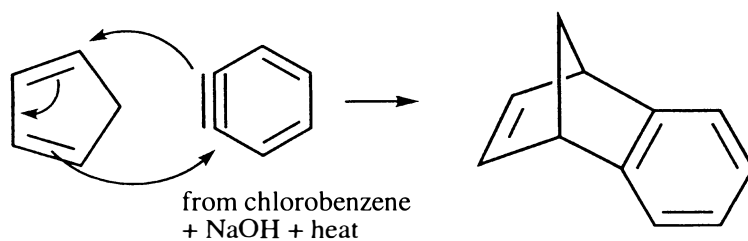
17-25 continued



17-26 Assume an acidic workup to each of these reactions to produce the phenol, not the phenoxide ion.

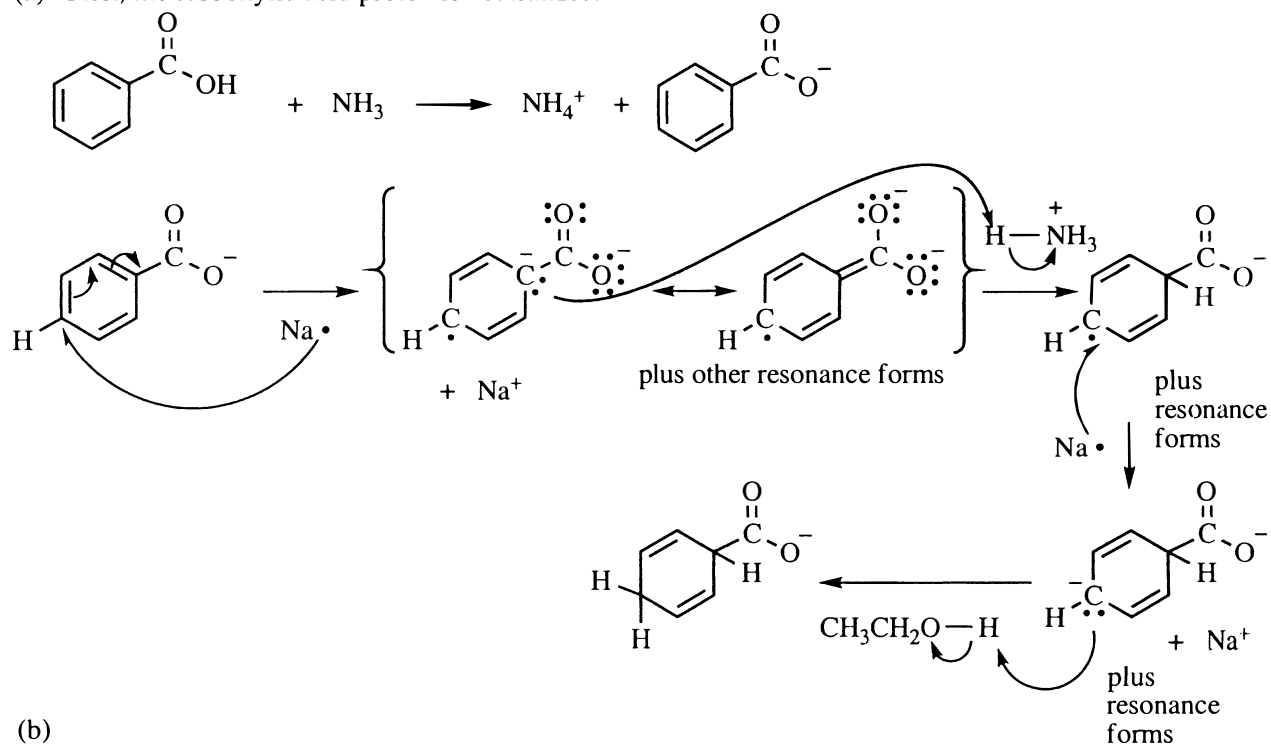


17-27

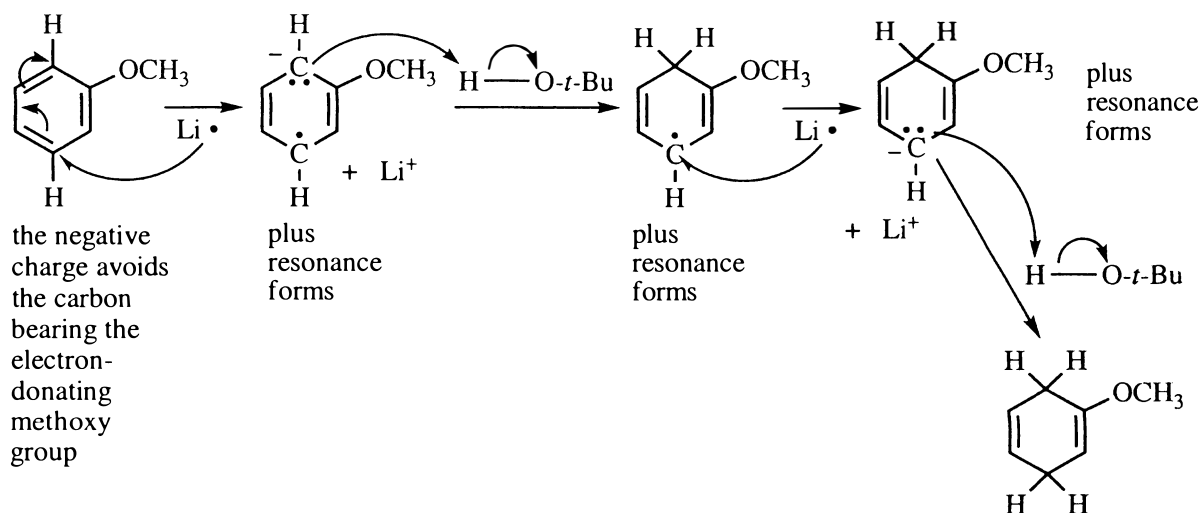


17-28

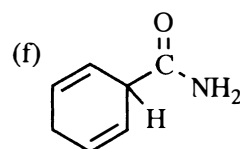
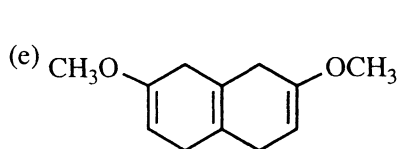
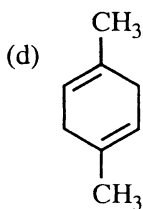
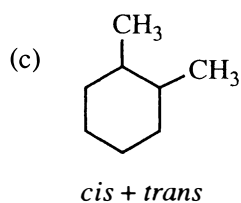
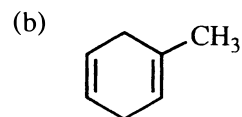
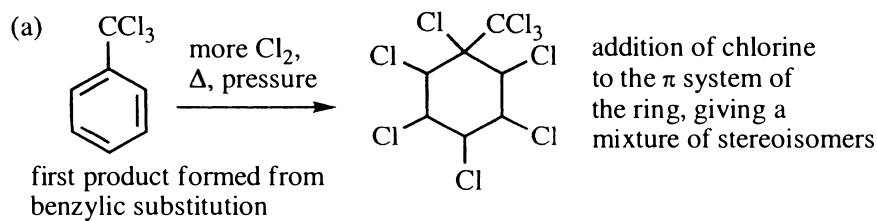
(a) First, the carboxylic acid proton is neutralized.



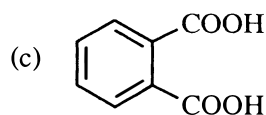
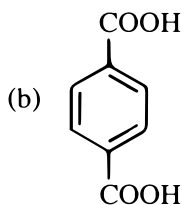
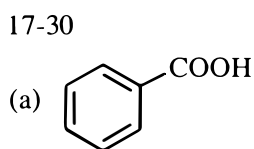
(b)



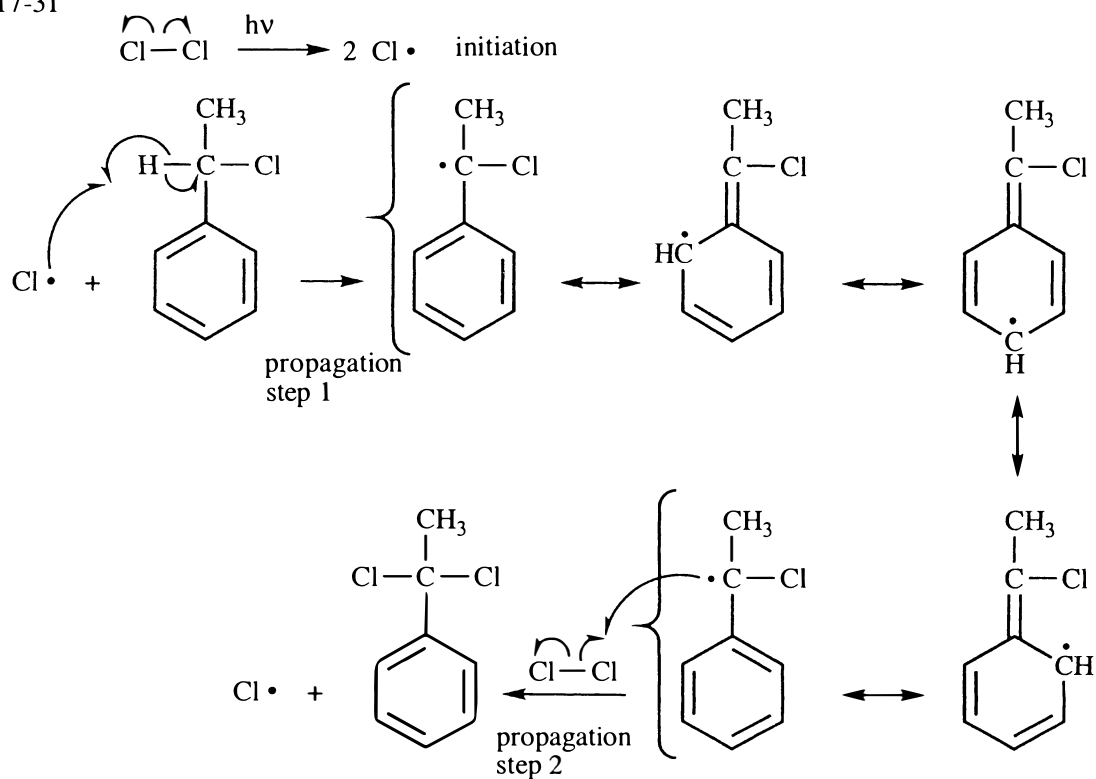
17-29



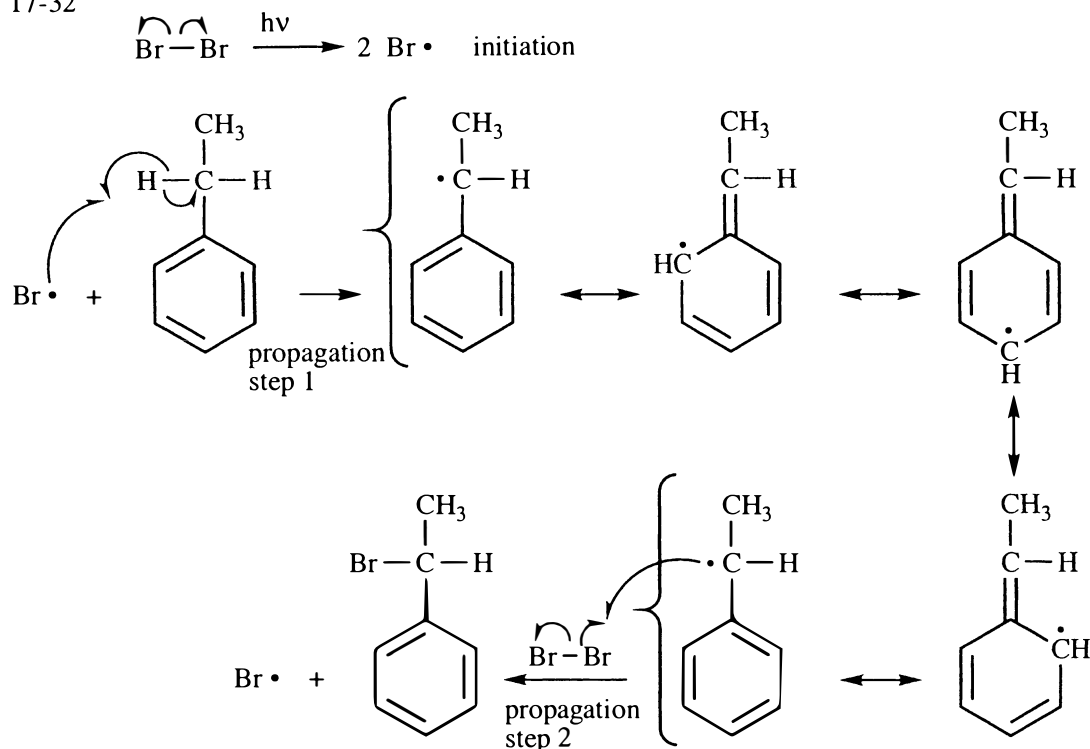
17-30



17-31



17-32



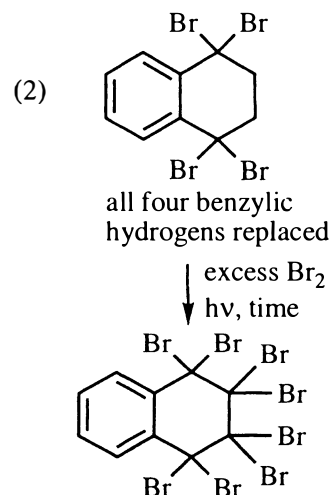
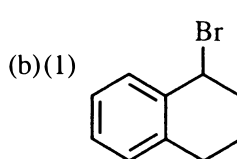
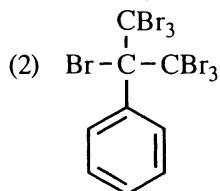
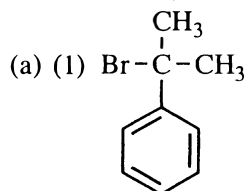
17-33 A statistical mixture would give 2 : 3 or 40% : 60% α to β . To calculate the relative reactivities, the percents must be corrected for the numbers of each type of hydrogen.

$$\alpha: \frac{56\%}{2\text{H}} = 28 \text{ relative reactivity}$$

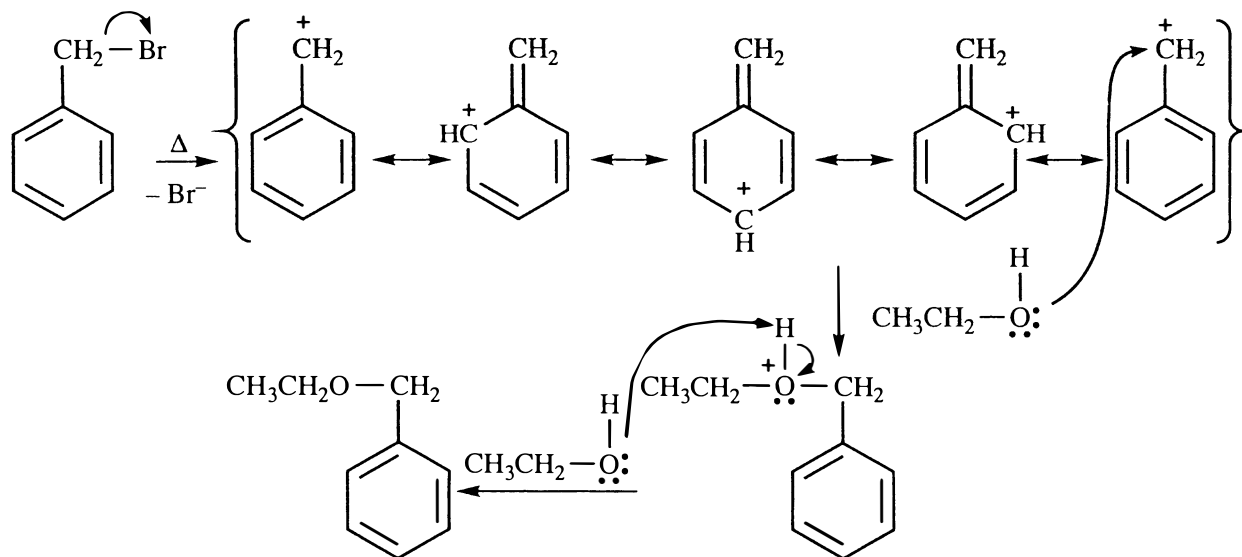
$$\beta: \frac{44\%}{3\text{H}} = 14.7 \text{ relative reactivity}$$

$$\text{The reactivity of } \alpha \text{ to } \beta \text{ is } \frac{28}{14.7} = 1.9 \text{ to } 1$$

17-34 Replacement of aliphatic hydrogens with bromine can be done under free radical substitution conditions, but reaction at aromatic carbons is unfavorable because of the very high energy of the aryl radical. Benzylic substitution is usually the only product observed.

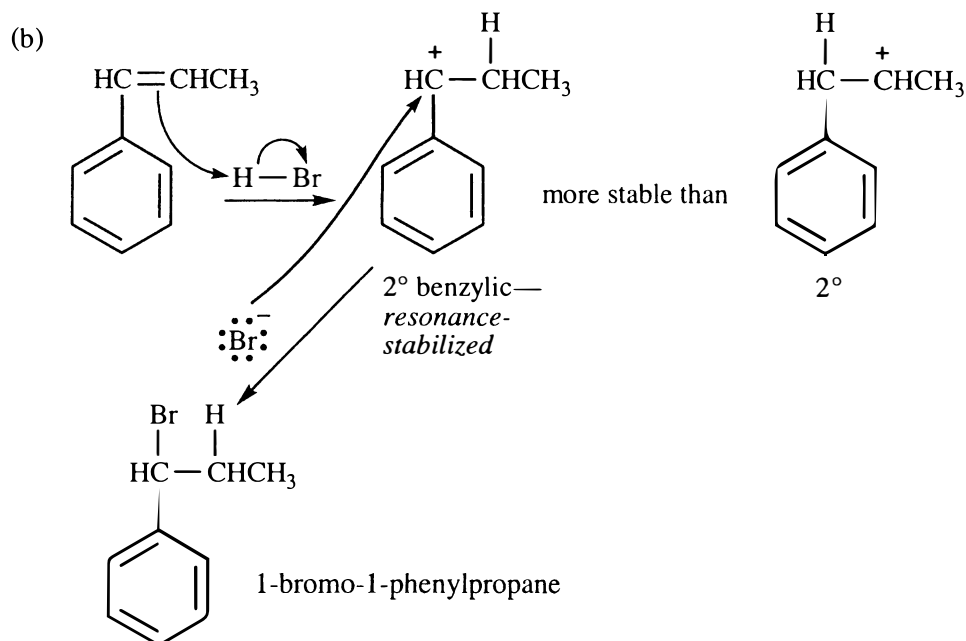


17-35



17-36

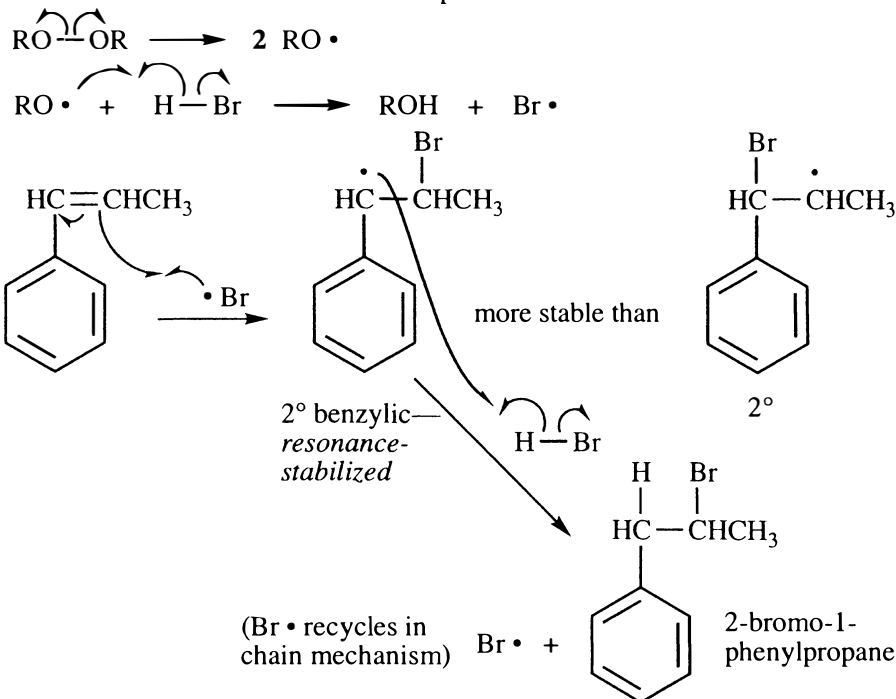
(a) Benzylic cations are stabilized by resonance and are much more stable than regular alkyl cations. The product is 1-bromo-1-phenylpropane.



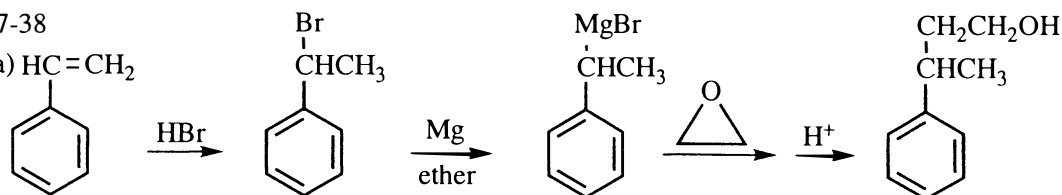
17-37

(a) The combination of HBr with a free-radical initiator generates bromine radicals and leads to anti-Markovnikov orientation. (Recall that whatever species adds *first* to an alkene determines orientation.) The product will be 2-bromo-1-phenylpropane.

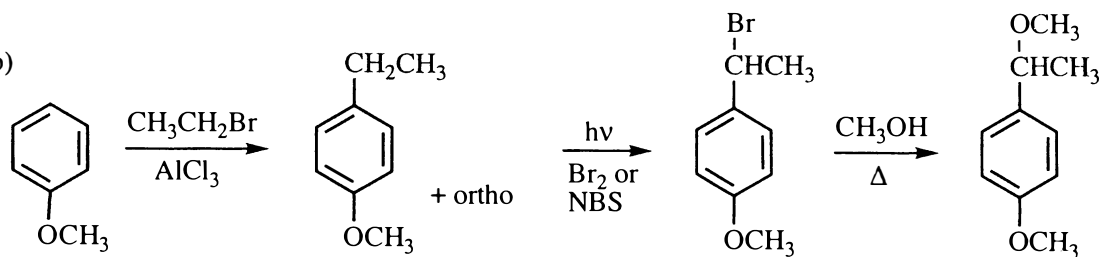
(b) Assume the free-radical initiator is a peroxide.



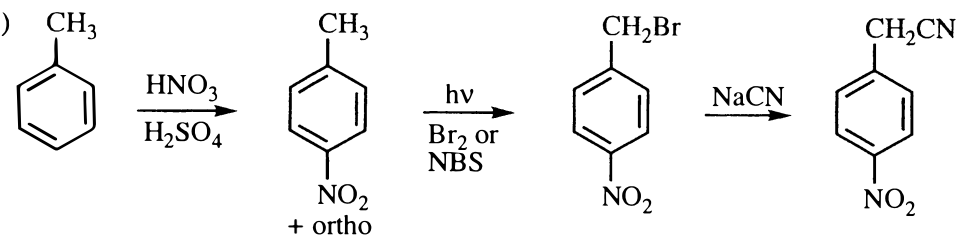
17-38

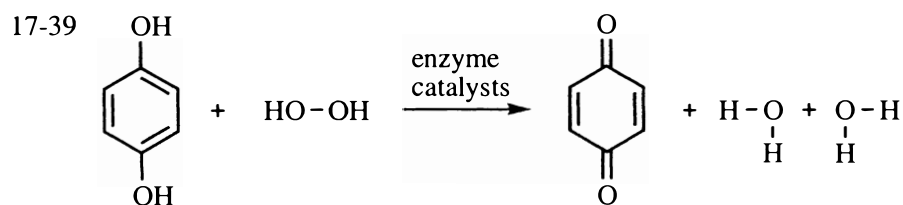
(a) $\text{HC}=\text{CH}_2$ 

(b)

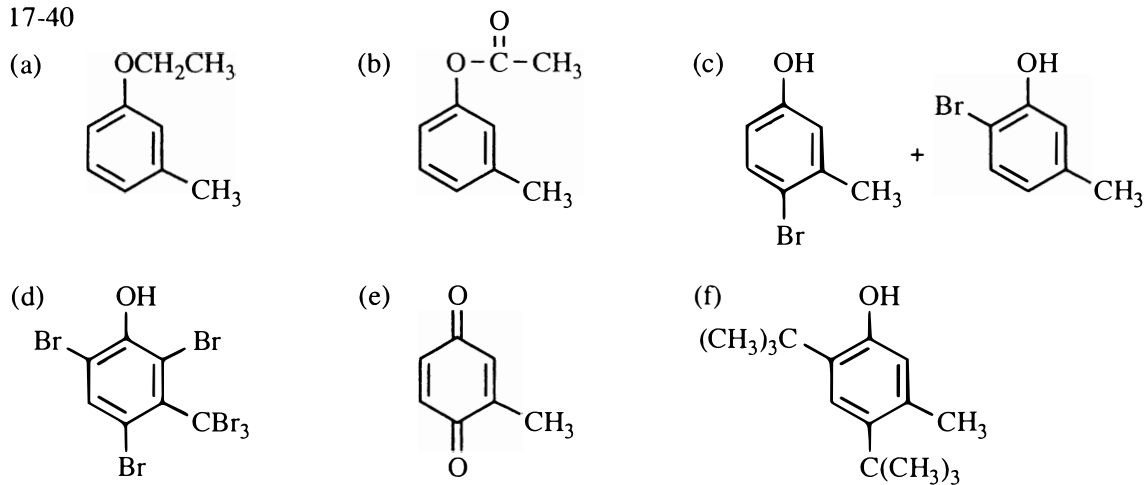


(c)

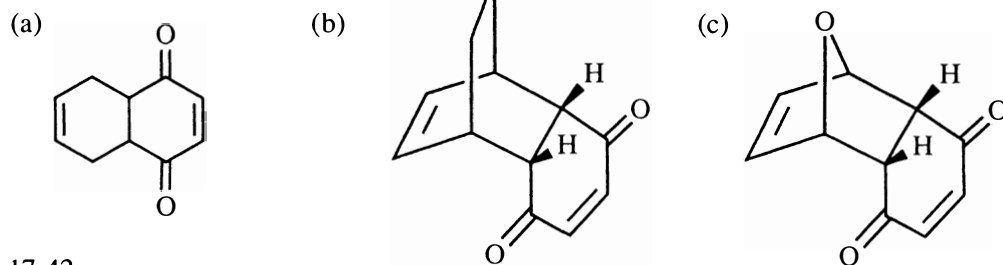




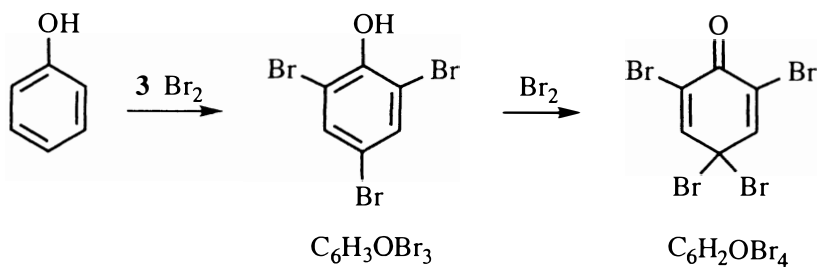
17-40



17-41

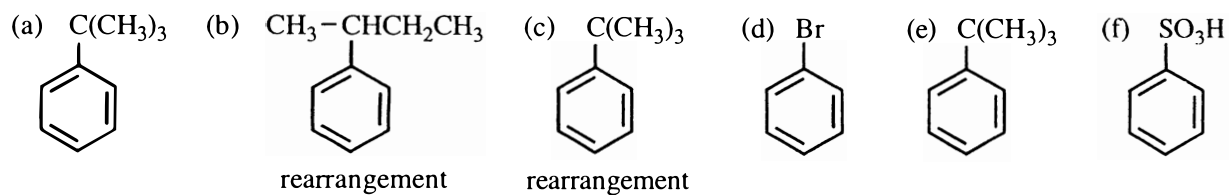


17-42

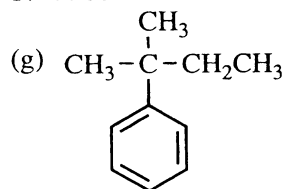


17-43 Please refer to solution 1-20, page 12 of this Solutions Manual.

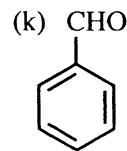
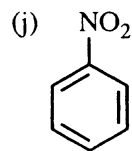
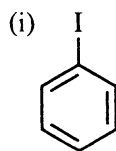
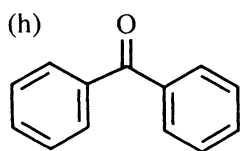
17-44



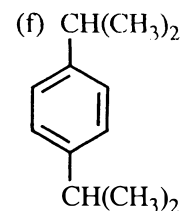
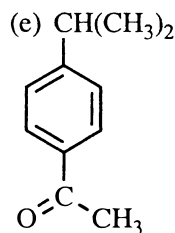
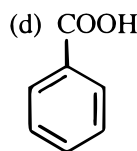
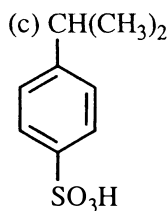
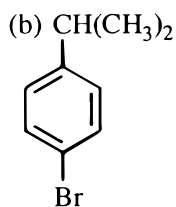
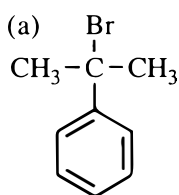
17-44 continued



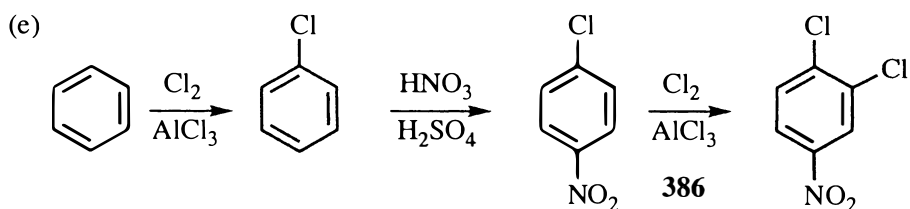
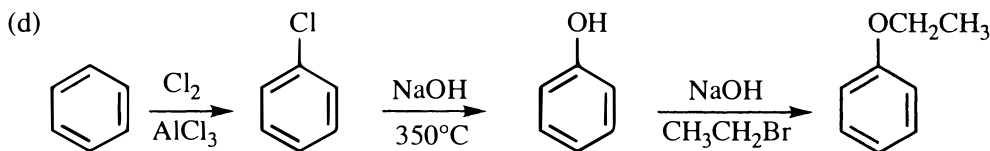
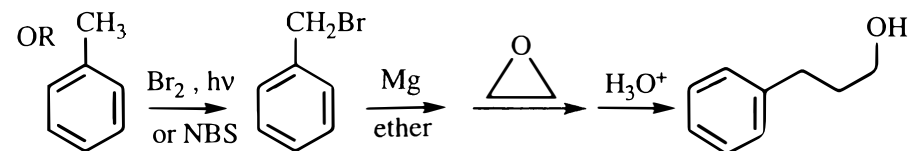
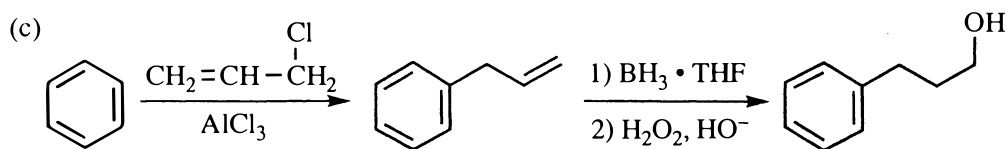
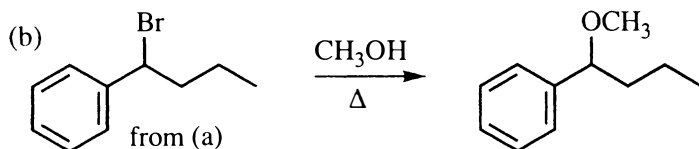
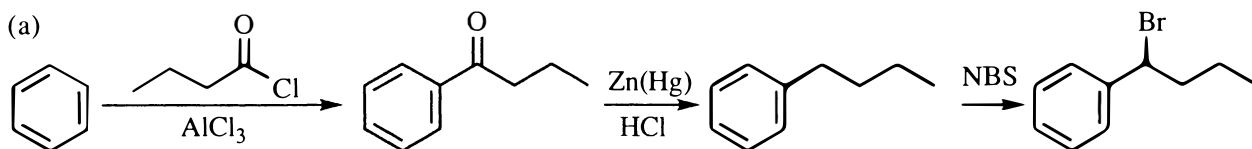
rearrangement



17-45 Products from substitution at the ortho position will be minor because of the steric bulk of the isopropyl group.

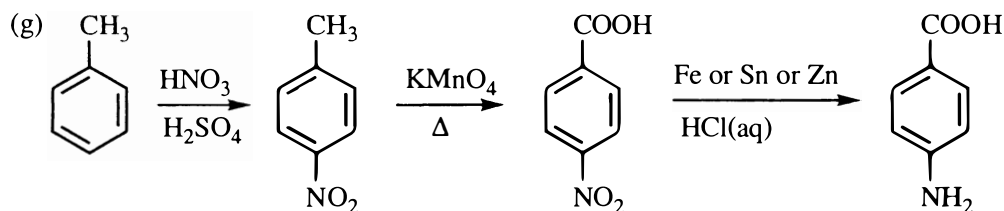
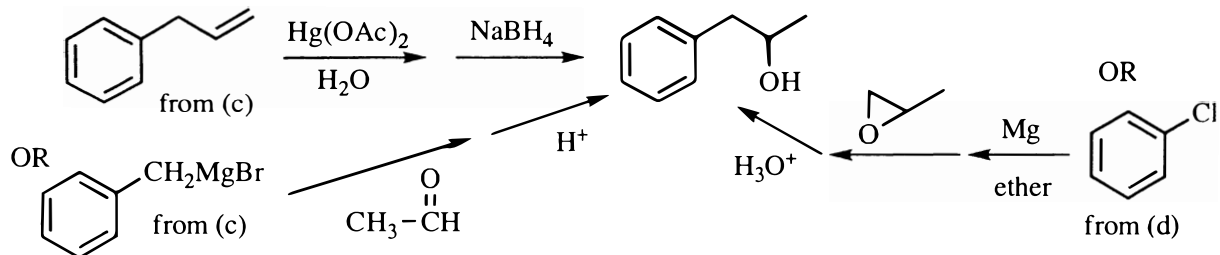


17-46

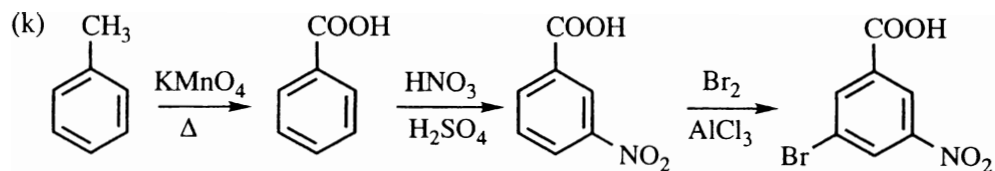
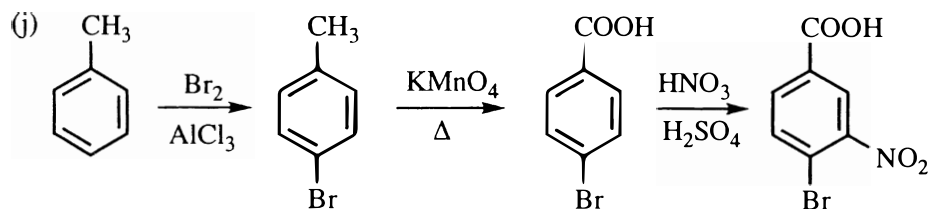
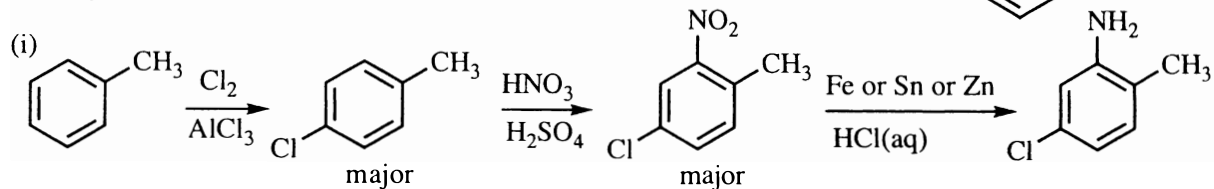
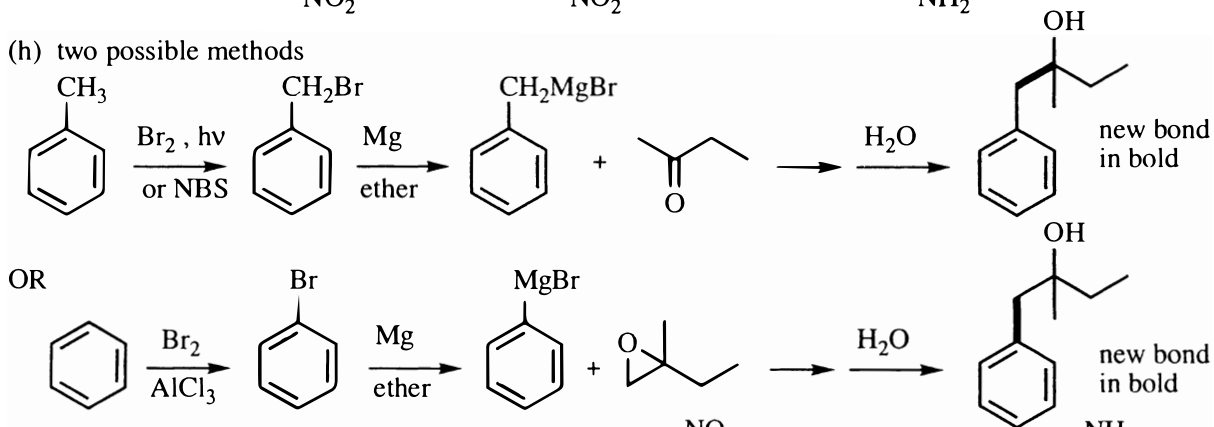


17-46 continued

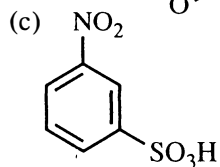
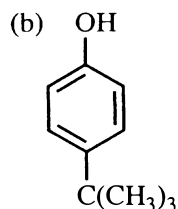
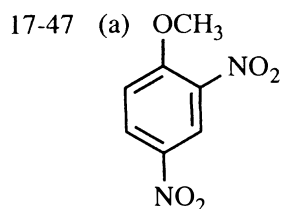
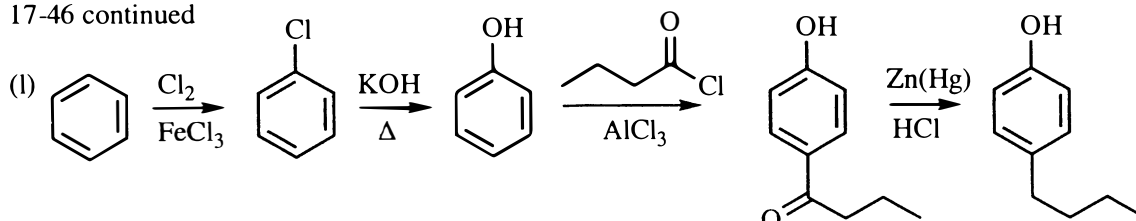
(f) three methods



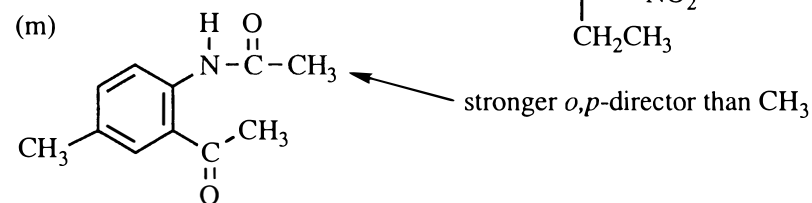
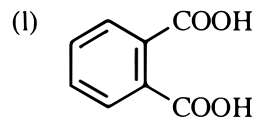
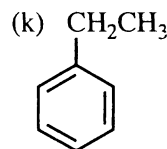
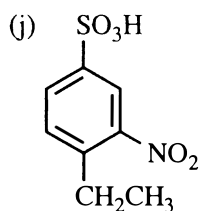
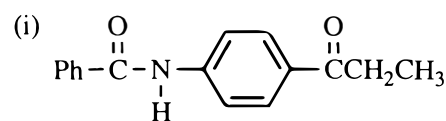
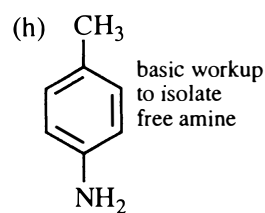
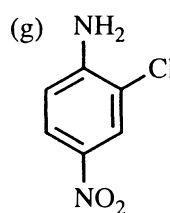
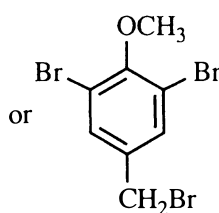
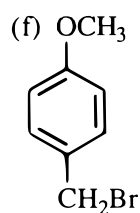
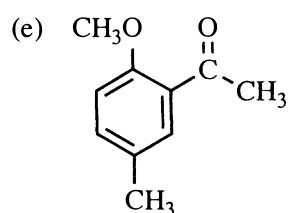
(h) two possible methods



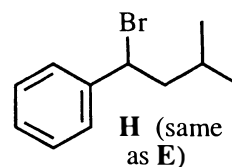
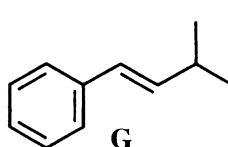
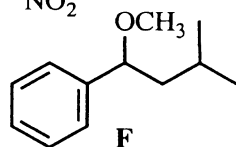
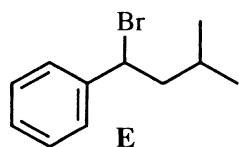
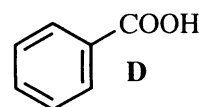
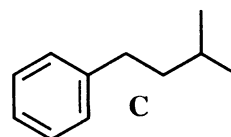
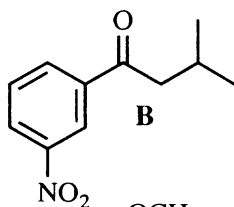
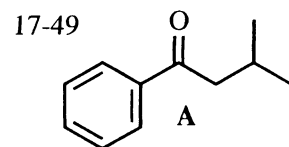
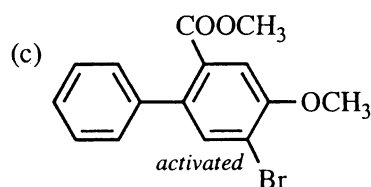
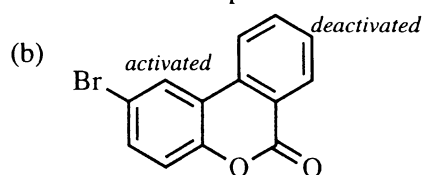
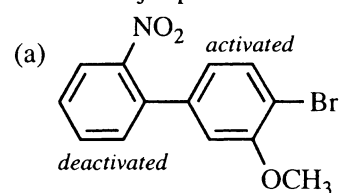
17-46 continued



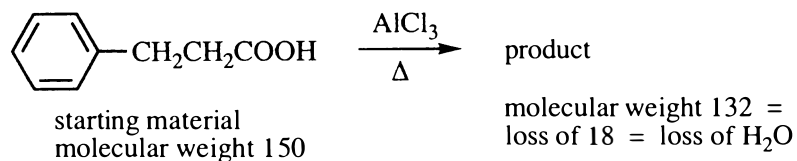
(d) no reaction: Friedel-Crafts acylation does not occur on rings with strong deactivating groups like NO₂



17-48 Major products are shown. Other isomers are possible.



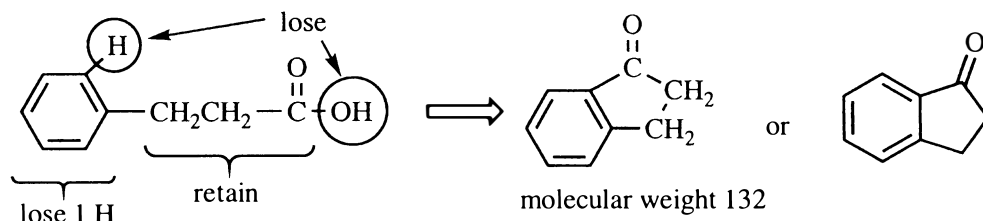
17-50



IR spectrum: The dominant peak is the carbonyl at 1710 cm^{-1} . No COOH stretch.

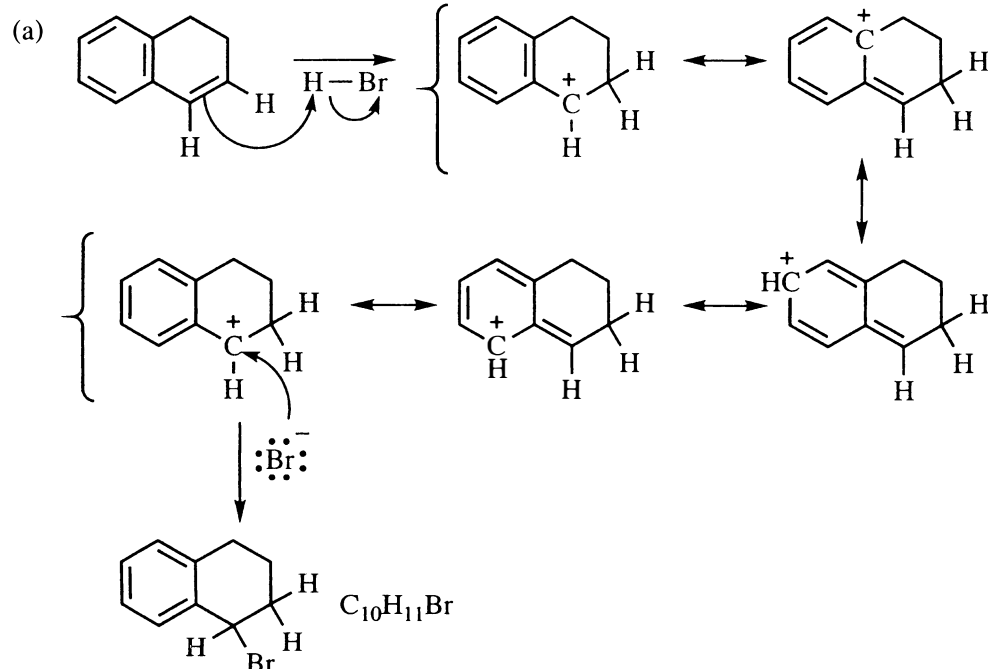
NMR spectrum: The splitting is complicated but the integration is helpful. In the region of δ 2.6-3.2, there are two signals each with integration value of 2H; these must be the two adjacent methylenes, CH_2CH_2 . The aromatic region from δ 7.3-7.8 has integration of 4H, so the ring must be disubstituted.

Carbon NMR: Four of the aromatic signals are tall, indicating C—H; two are short, with no attached hydrogens, also showing a disubstituted benzene. Also indicated are carbons in a carbonyl and two methylenes.



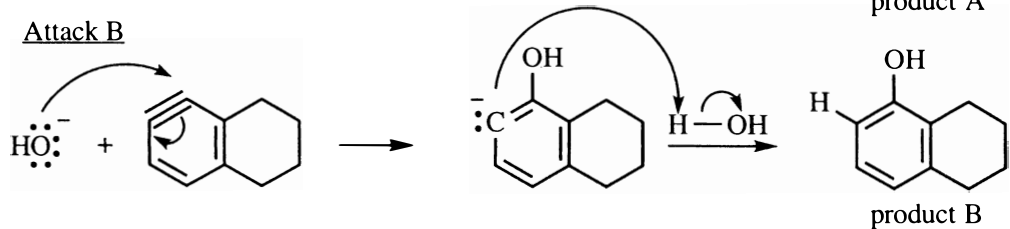
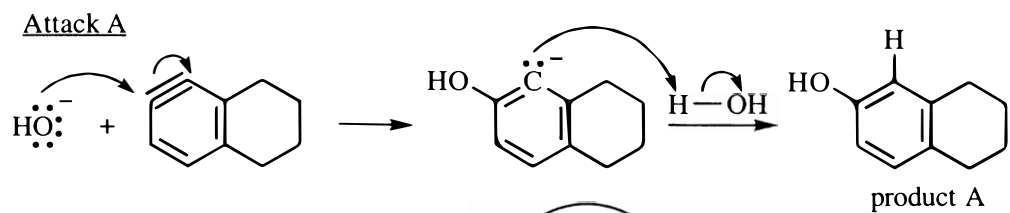
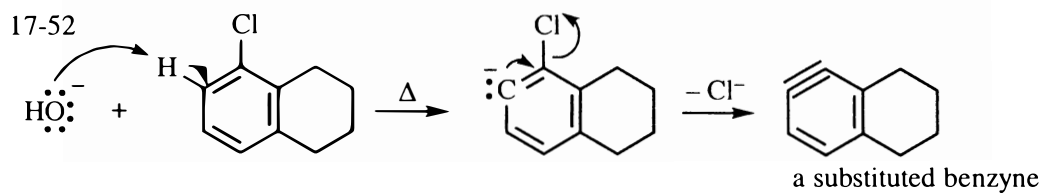
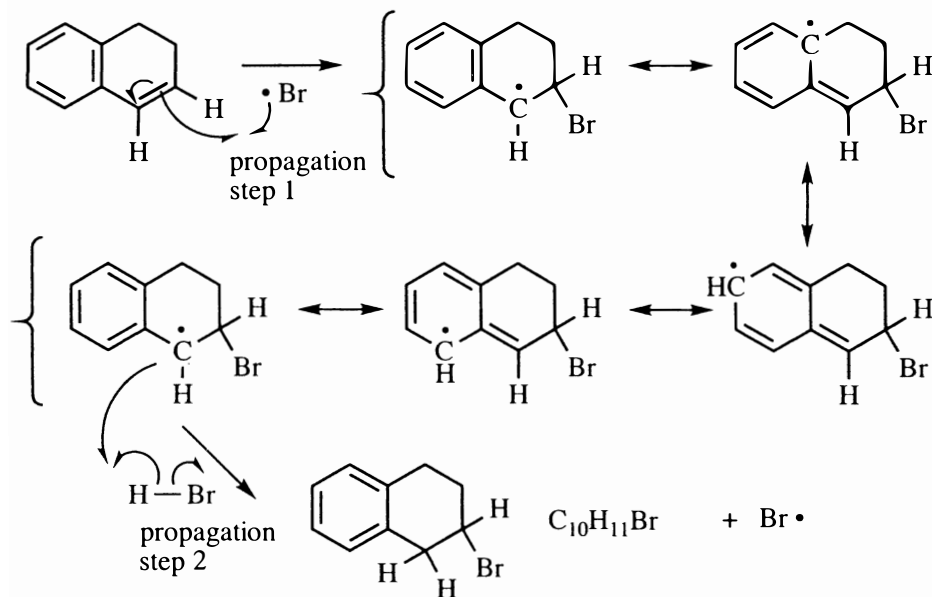
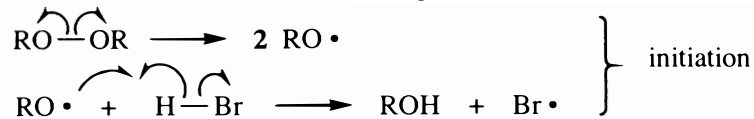
The product must be the cyclized ketone, formed in an intramolecular Friedel-Crafts acylation.

17-51

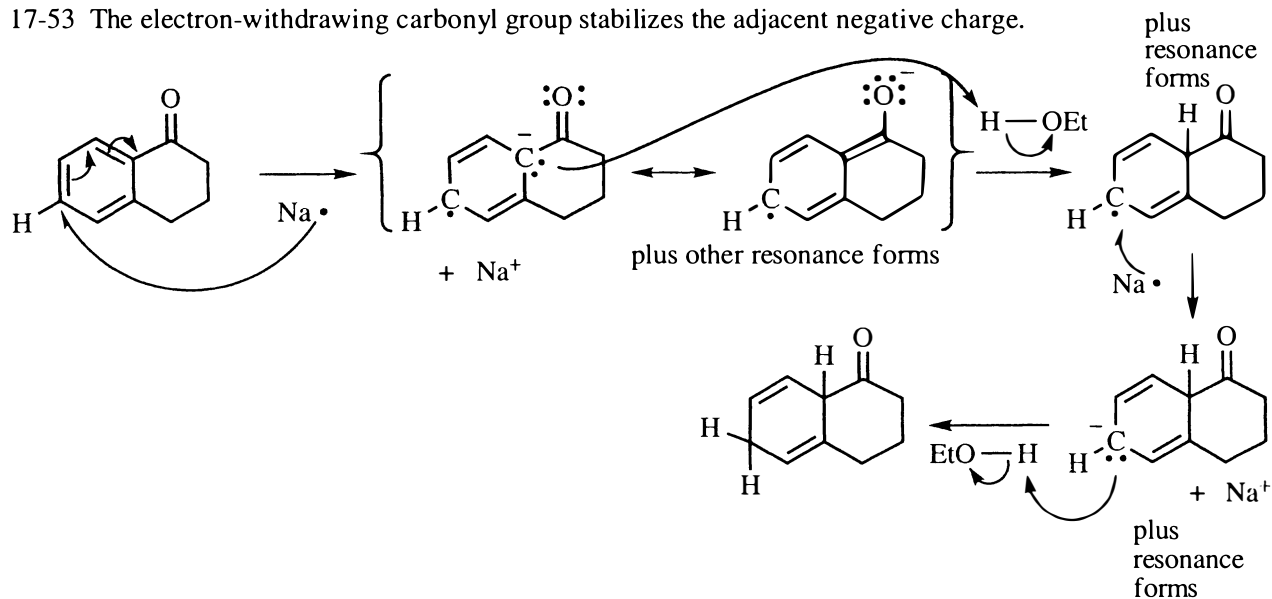


17-51 continued

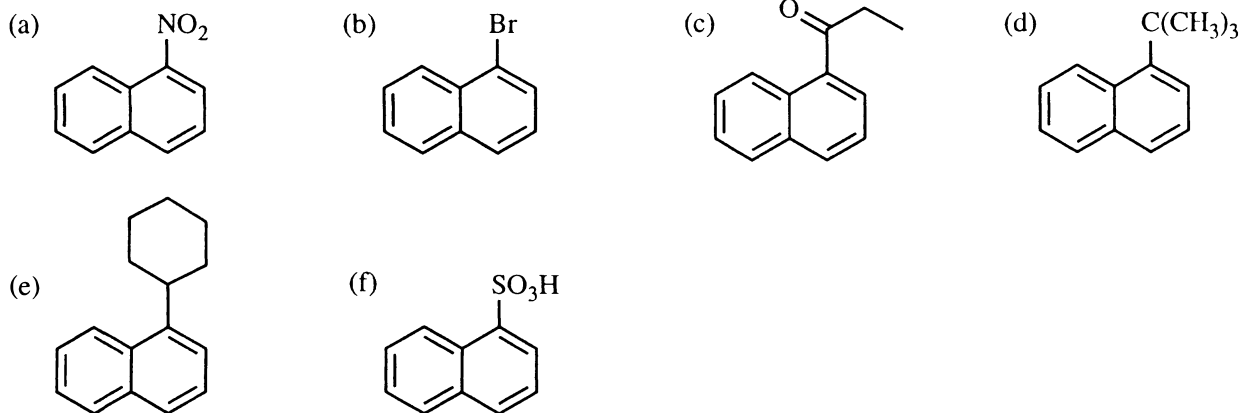
(b) Assume the free-radical initiator is a peroxide.



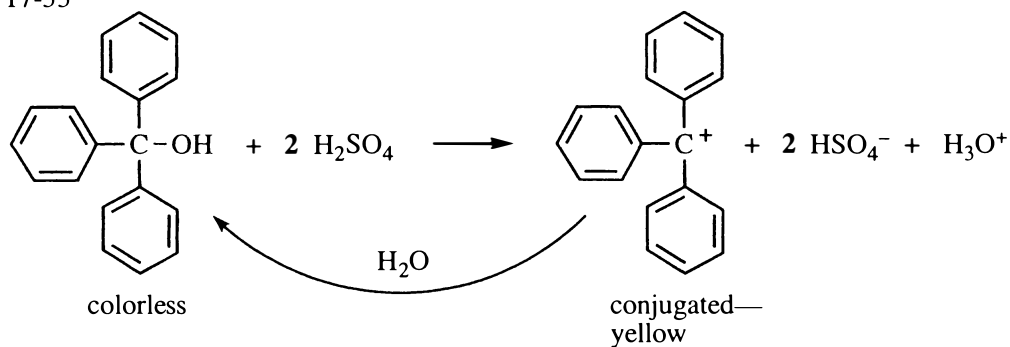
17-53 The electron-withdrawing carbonyl group stabilizes the adjacent negative charge.



17-54

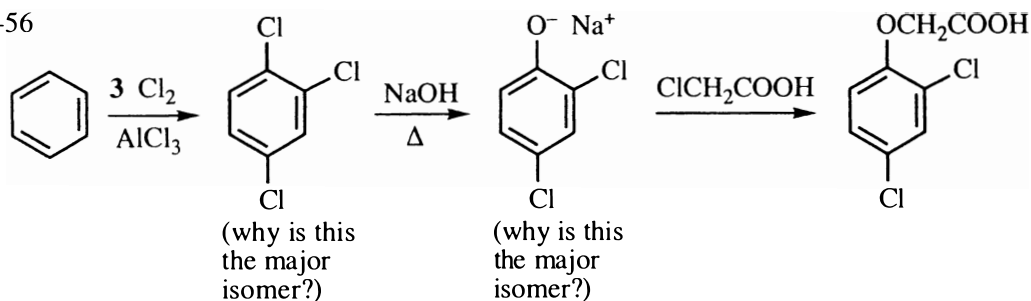


17-55



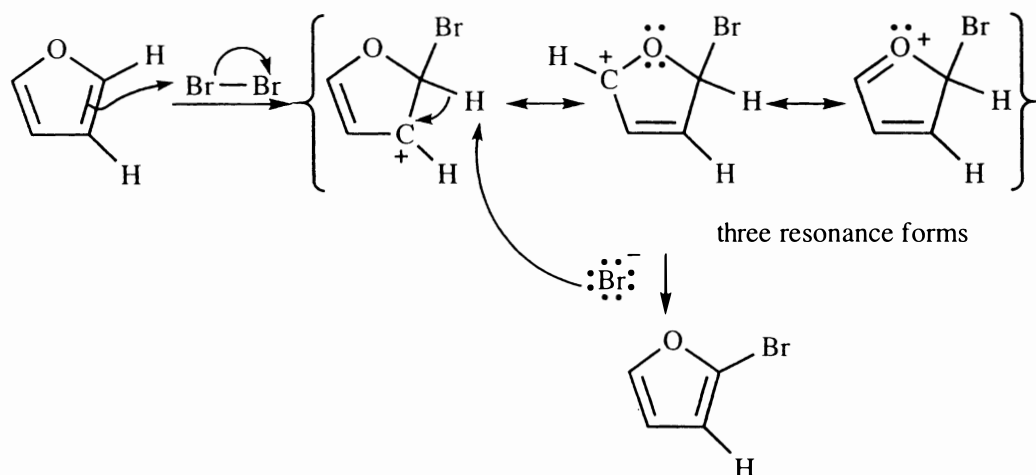
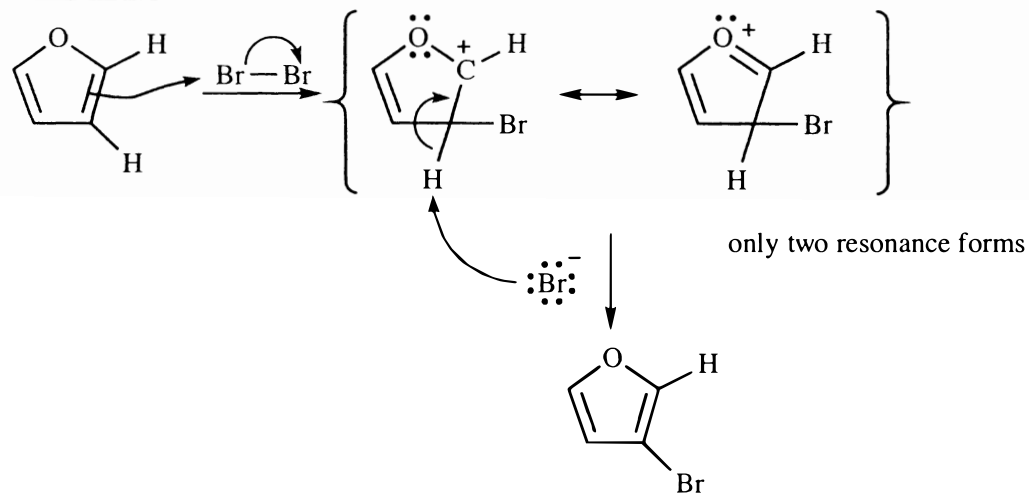
Concentrated sulfuric acid "dehydrates" the alcohol, producing a highly conjugated, colored carbocation, and protonates the water to prevent the reverse reaction. Upon adding more water, however, there are too many water molecules for the acid to protonate, and triphenylmethanol is regenerated.

17-56



17-57

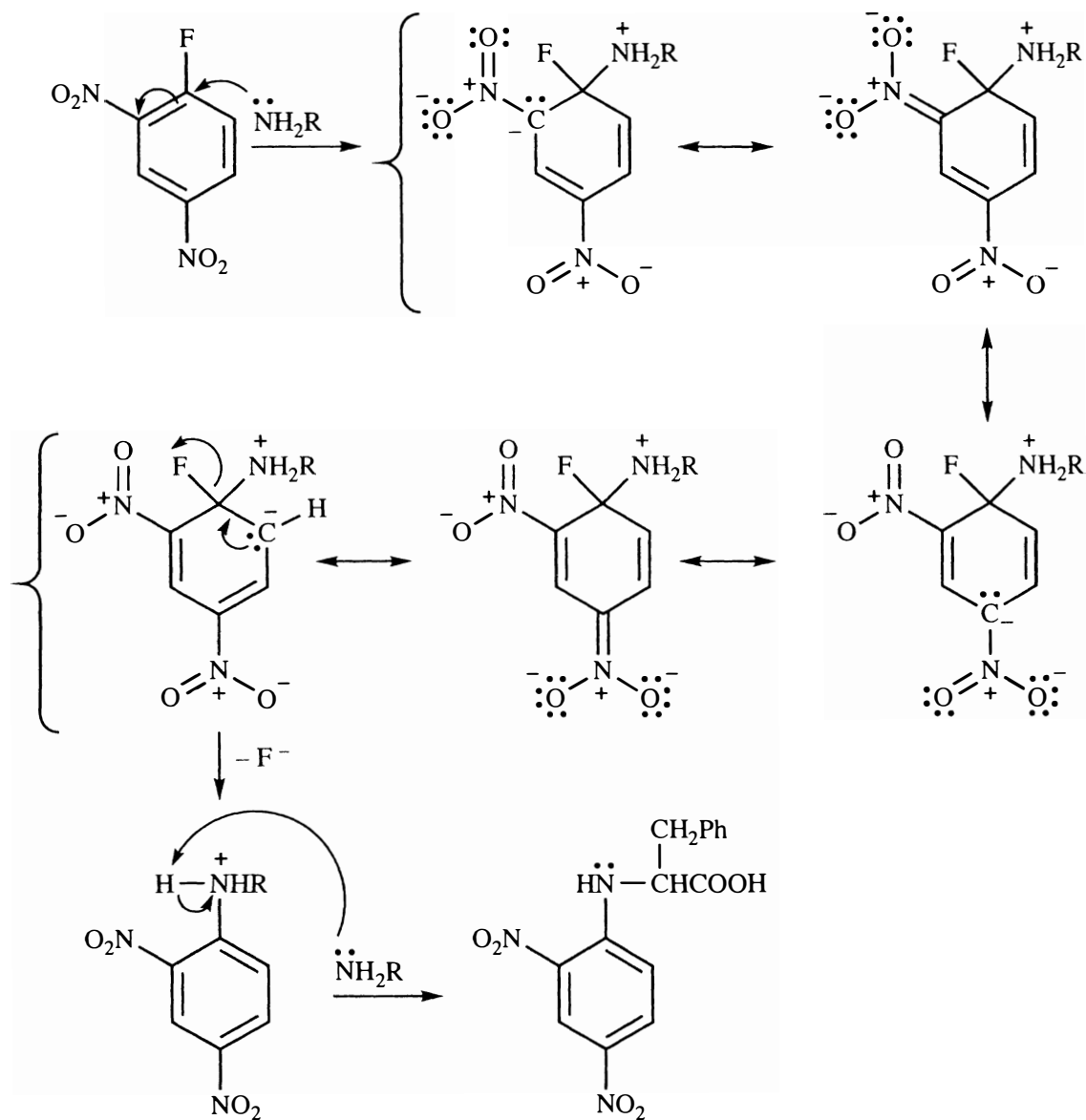
(a)

bromination at C-2bromination at C-3

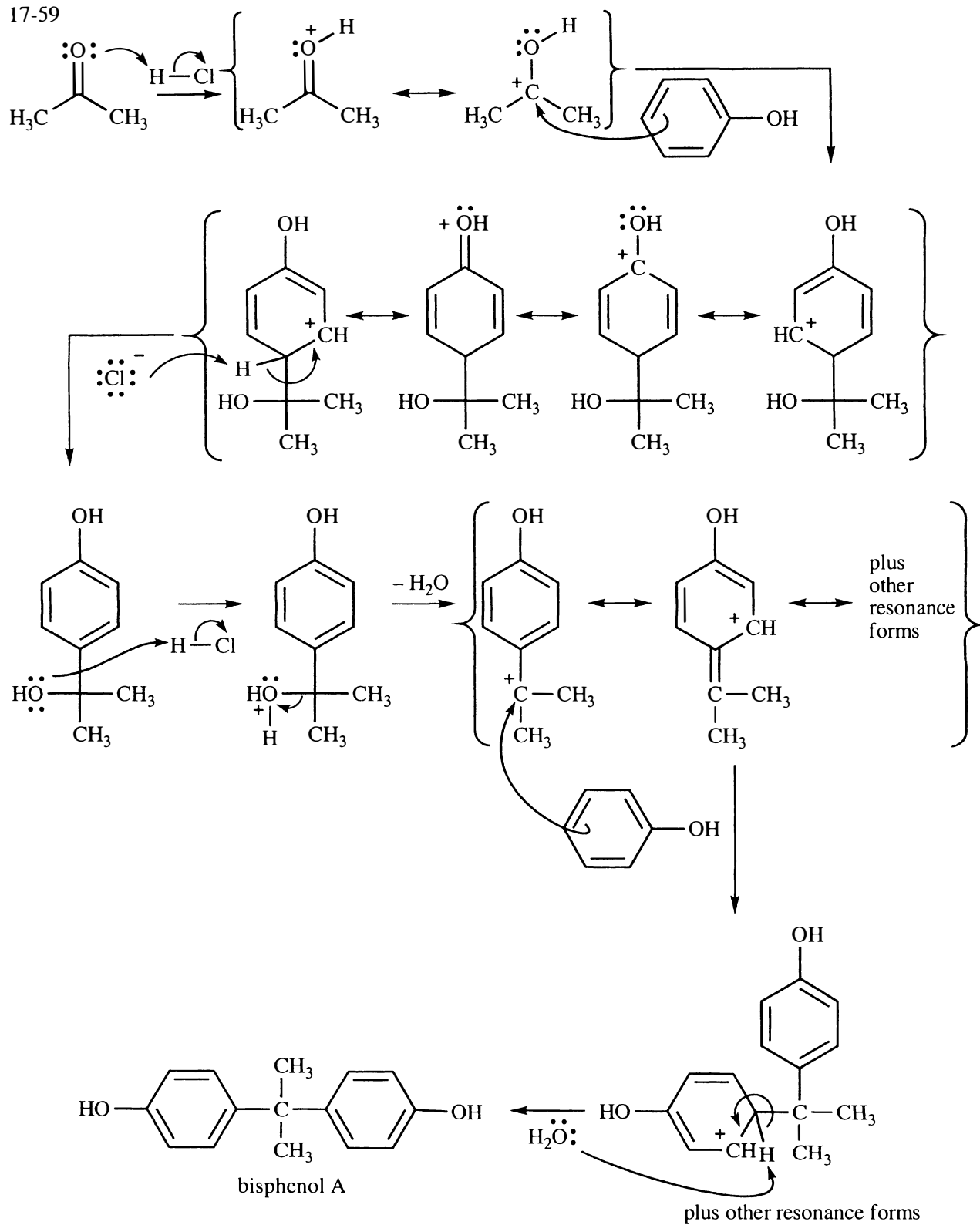
(b) Attack at C-2 gives an intermediate stabilized by three resonance forms, as opposed to only two resonance forms stabilizing attack at C-3. Bromination at C-2 will occur more readily.

17-58

abbreviate $\text{PhCH}_2\text{—}\overset{\text{NH}_2}{\underset{|}{\text{CH}}}\text{COOH}$ as $\overset{\text{NH}_2}{\underset{|}{\text{R}}}$
 phenylalanine



17-59

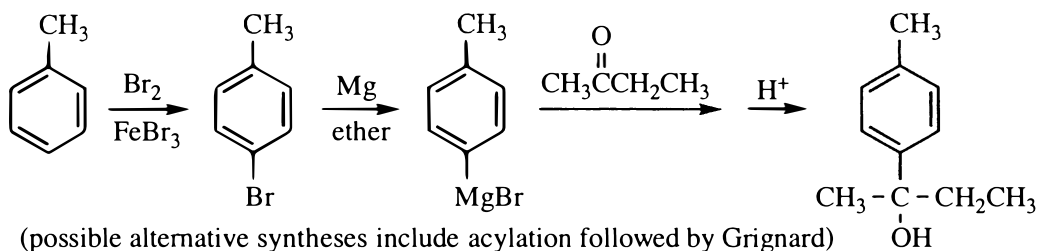


17-60

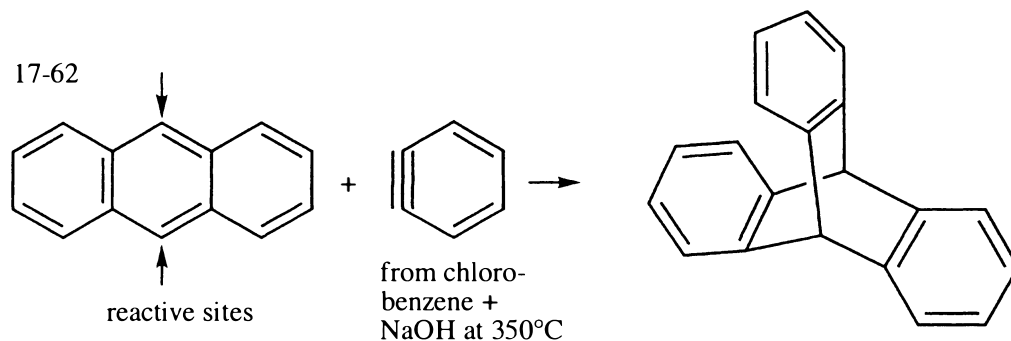
(a) This is an example of kinetic versus thermodynamic control of a reaction. At low temperature, the kinetic product predominates: in this case, almost a 1 : 1 mixture of ortho and para. These two isomers must be formed at approximately equal rates at 0° C. At 100° C, however, enough energy is provided for the *desulfonation* to occur rapidly; the large excess of the para isomer indicates the para is more stable, even though it is formed initially at the same rate as the ortho.

(b) The product from the 0° C reaction will equilibrate as it is warmed, and at 100° C will produce the same ratio of products as the reaction which was run initially at 100° C.

17-61

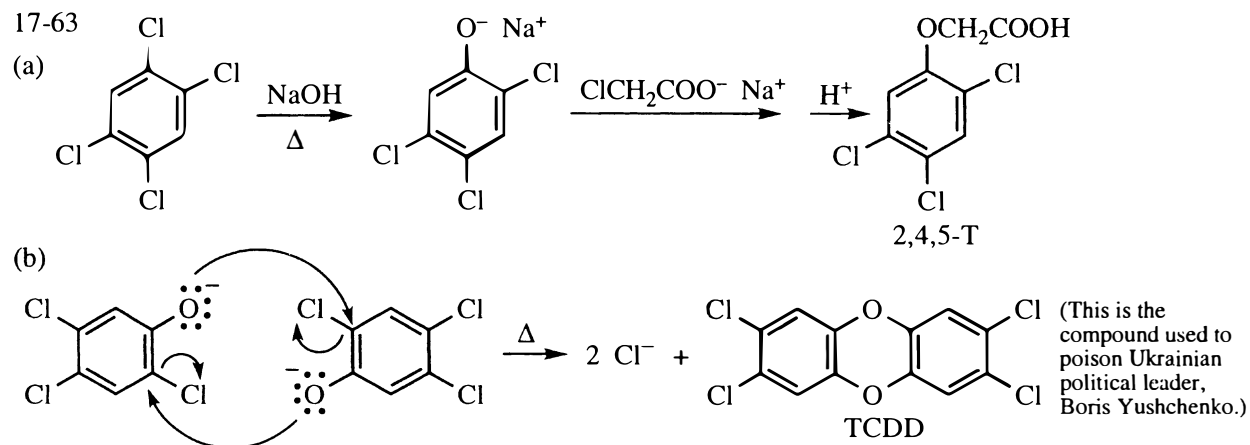


17-62



As we saw in Chapter 16, the carbons of the center ring of anthracene are susceptible to electrophilic addition, leaving two isolated benzene rings on the ends. Benzyne is such a reactive dienophile that the reluctant anthracene is forced into a Diels-Alder reaction.

17-63

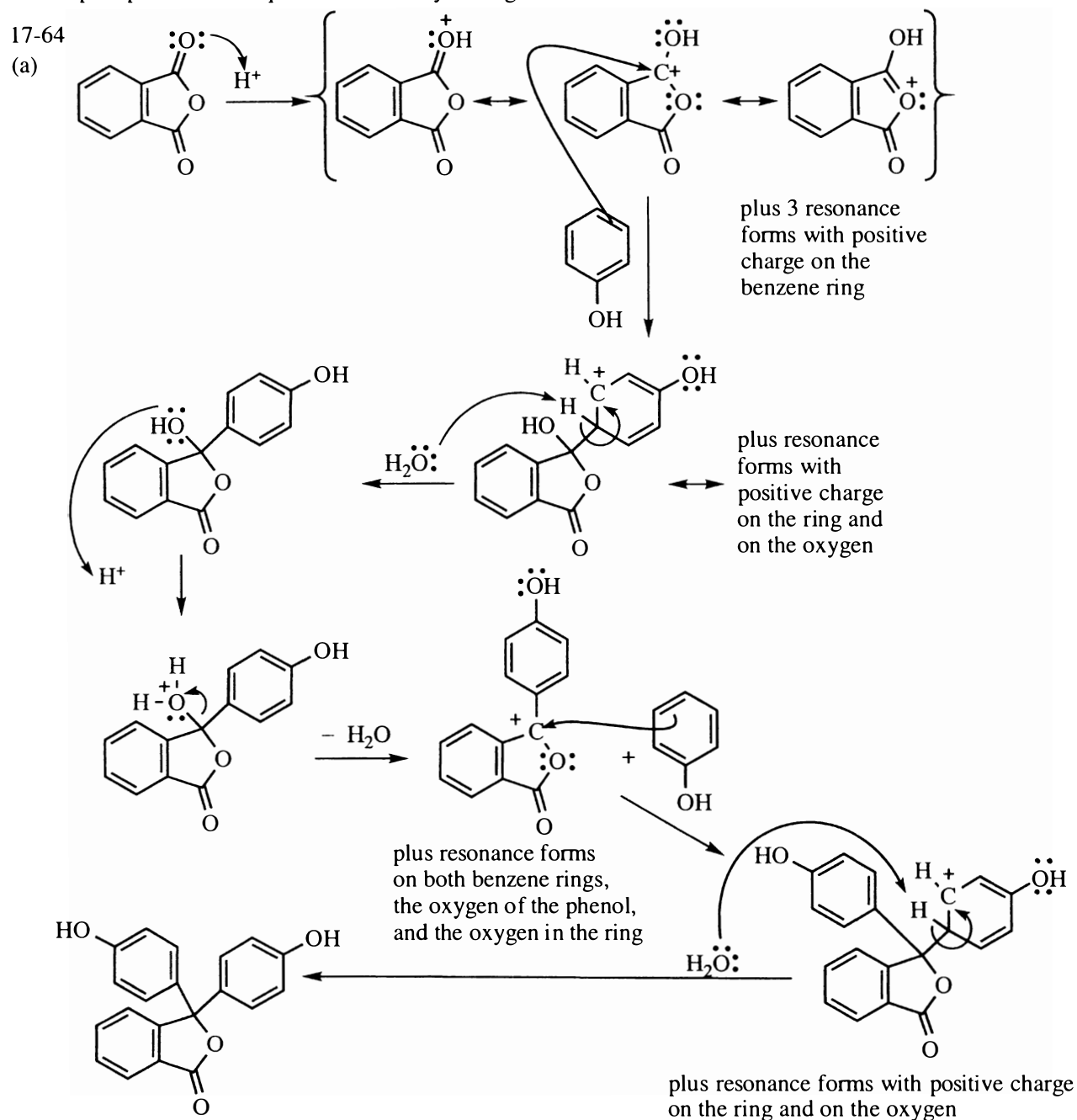


Two nucleophilic aromatic substitutions form a new six-membered ring. (Though not shown here, this reaction would follow the standard addition-elimination mechanism.)

17-63 continued

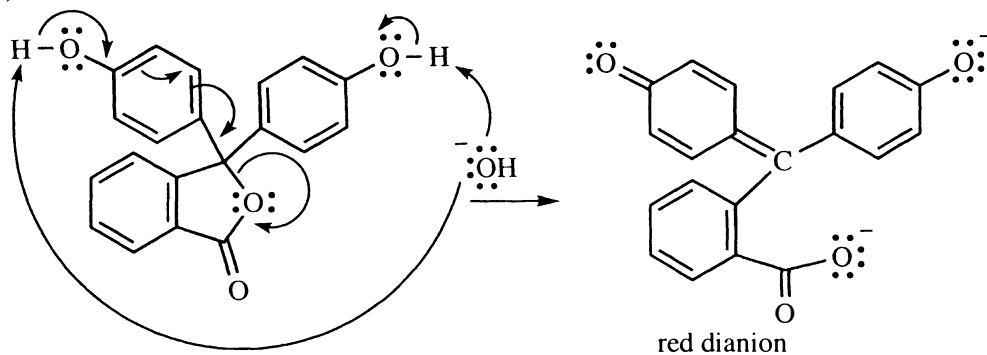
(c) To minimize formation of TCDD during synthesis: 1) keep the solutions dilute; 2) avoid high temperature; 3) replace chloroacetate with a more reactive molecule like bromoacetate or iodoacetate; 4) add an excess of the haloacetate.

To separate TCDD from 2,4,5-T at the end of the synthesis, take advantage of the acidic properties of 2,4,5-T. The 2,4,5-T will dissolve in an aqueous solution of a weak base like NaHCO_3 . The TCDD will remain insoluble and can be filtered or extracted into an organic solvent like ether or dichloromethane. The 2,4,5-T can be precipitated from aqueous solution by adding acid.

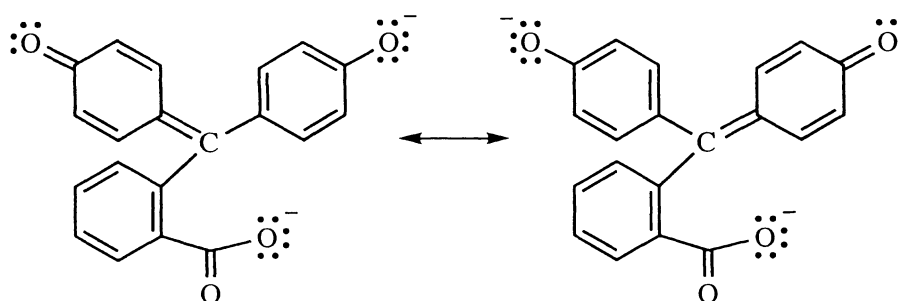


17-64 continued

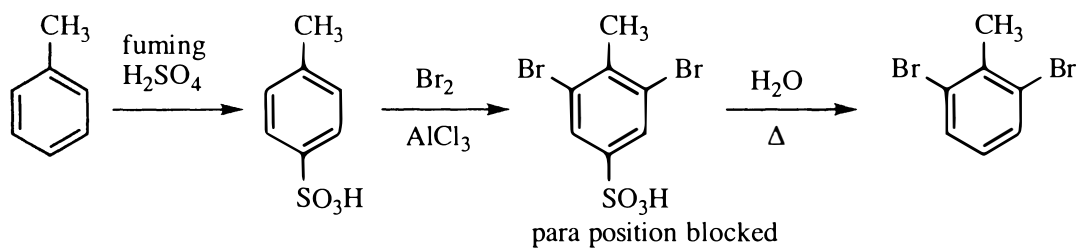
(b)



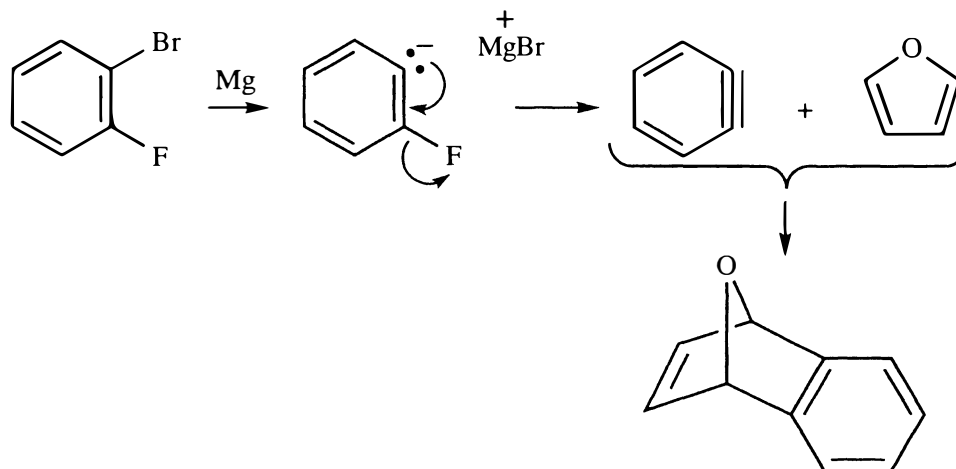
(c)



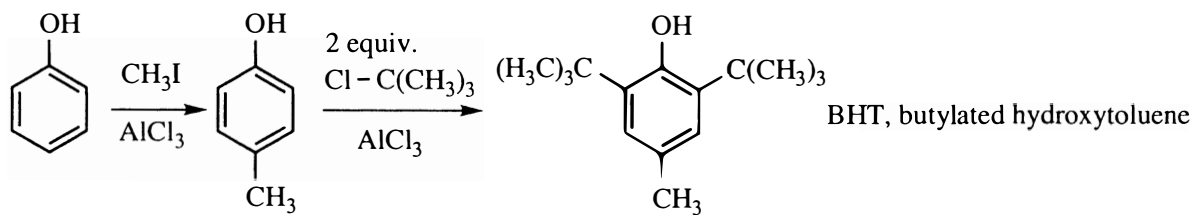
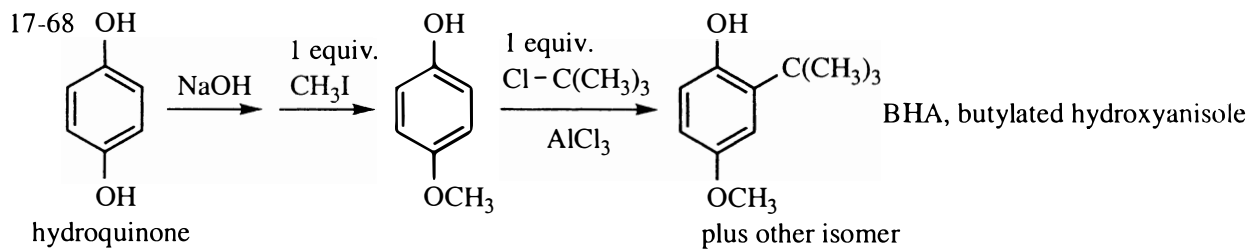
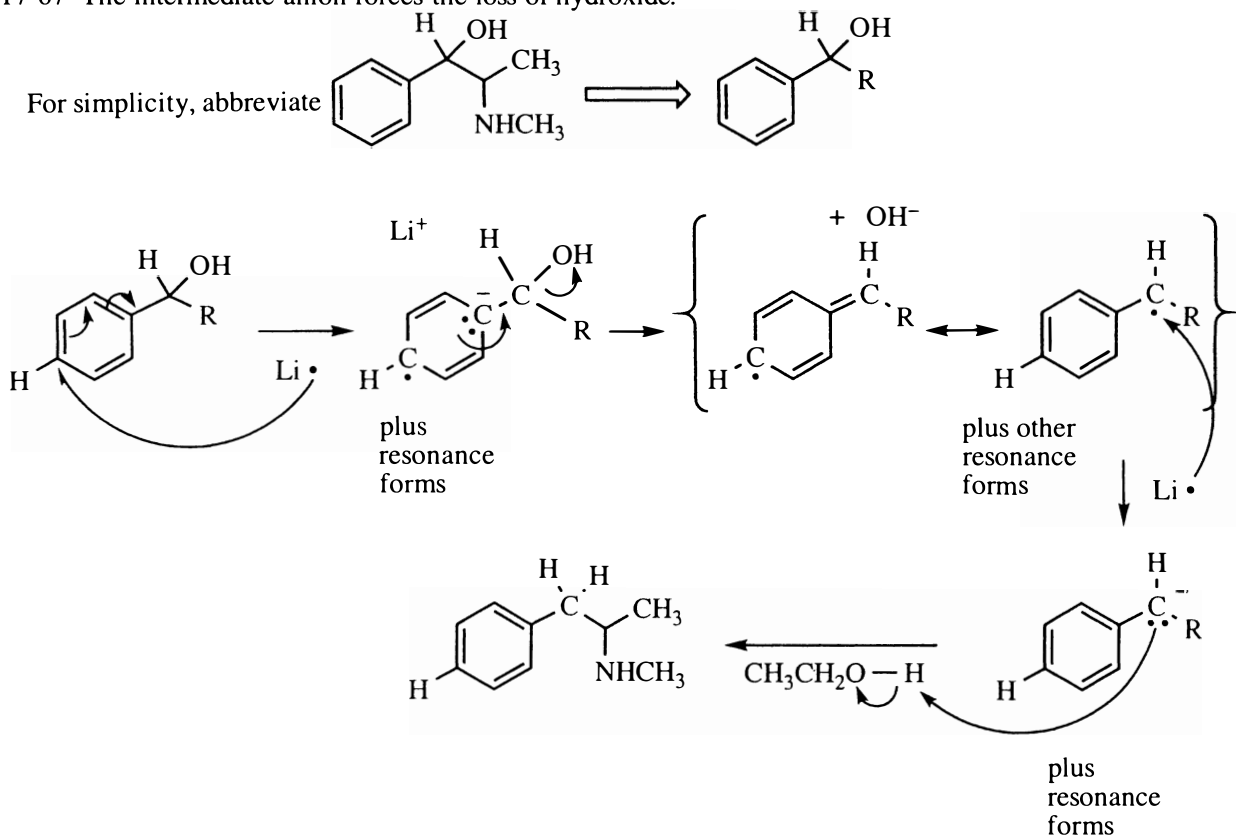
17-65



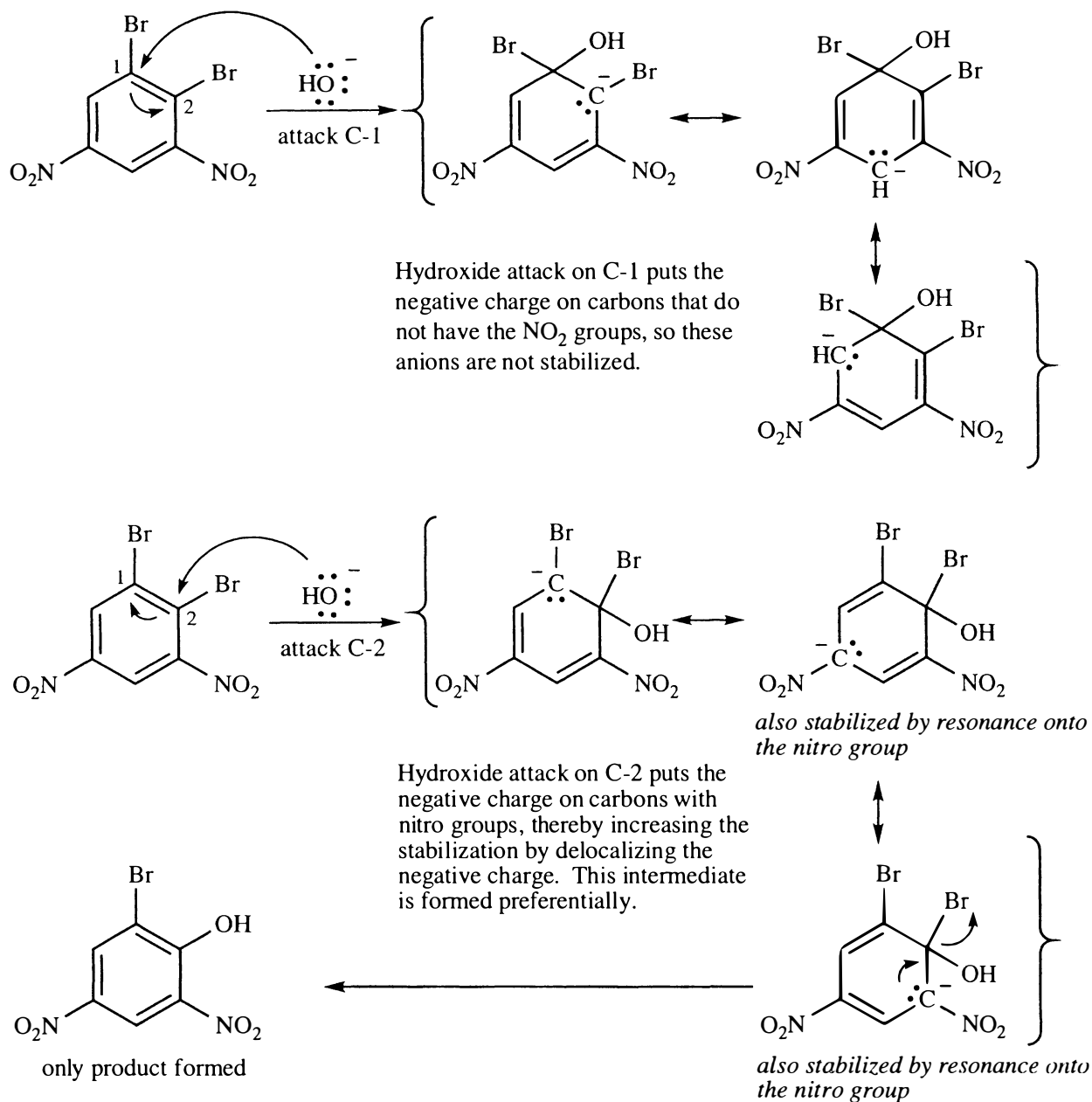
17-66 A benzyne must have been generated from the Grignard reagent.



17-67 The intermediate anion forces the loss of hydroxide.



17-69 Solve the problem by writing the mechanism. (See the solution to problem 17-25(a) for an identical mechanism.)



CHAPTER 18—KETONES AND ALDEHYDES

18-1

- (a) 5-hydroxyhexan-3-one; ethyl β -hydroxypropyl ketone
- (b) 3-phenylbutanal; β -phenylbutyraldehyde
- (c) *trans*-2-methoxycyclohexanecarbaldehyde (or (*R,R*) if you named this enantiomer); no common name
- (d) 6,6-dimethylcyclohexa-2,4-dienone; no common name

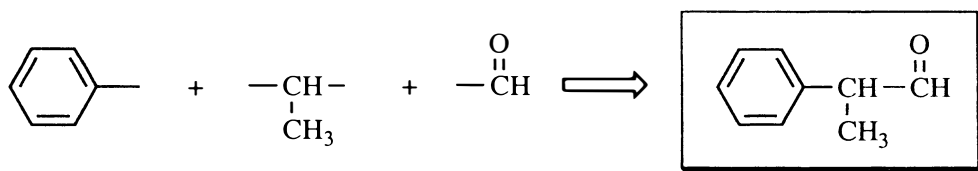
18-2

- (a) $C_9H_{10}O \Rightarrow$ 5 elements of unsaturation

1H doublet (very small coupling constant) at δ 9.7 $\Rightarrow$ aldehyde hydrogen, next to CH

5H multiple peaks at δ 7.2-7.4 $\Rightarrow$ monosubstituted benzene

1H multiplet at δ 3.6 and 3H doublet at δ 1.4 $\Rightarrow$ CHCH₃



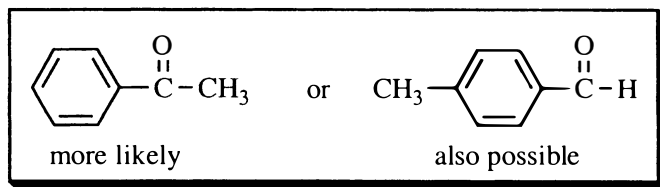
The splitting of the hydrogen on carbon-2, next to the aldehyde, is worth examining. In its overall shape, it looks like a quartet due to the splitting from the adjacent CH₃. A closer examination of the peaks shows that each peak of the quartet is split into two peaks: this is due to the splitting from the aldehyde hydrogen. The aldehyde hydrogen and the methyl hydrogens are not equivalent, so it is to be expected that the coupling constants will not be equal. If a hydrogen is coupled to different neighboring hydrogens by different coupling constants, they must be considered separately, just as you would by drawing a splitting tree for each type of adjacent hydrogen.

- (b) $C_8H_8O \Rightarrow$ 5 elements of unsaturation

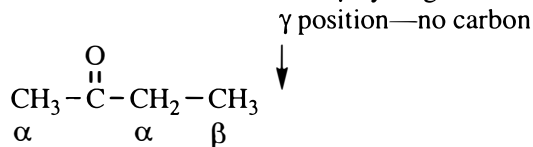
cluster of 4 peaks at δ 128-145 $\Rightarrow$ mono- or para-substituted benzene ring

peak at δ 197 $\Rightarrow$ carbonyl carbon (the small peak height suggests a ketone rather than an aldehyde)

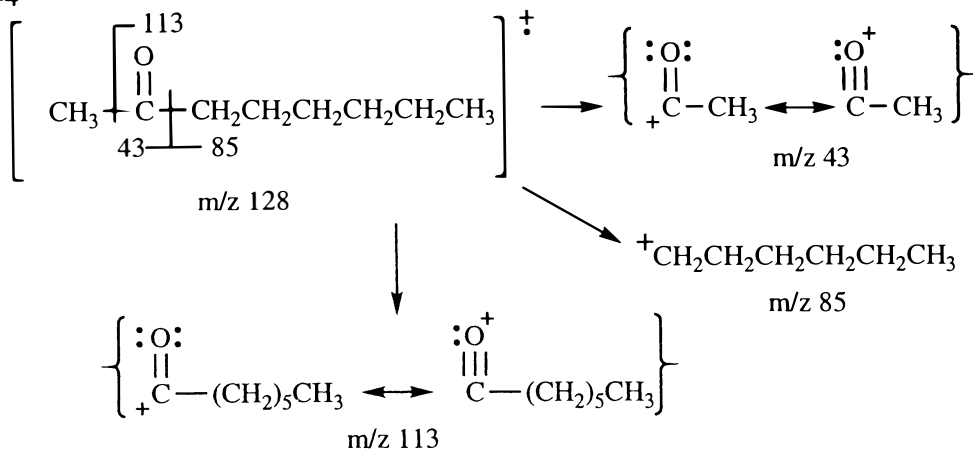
peak at δ 26 $\Rightarrow$ methyl next to carbonyl or benzene



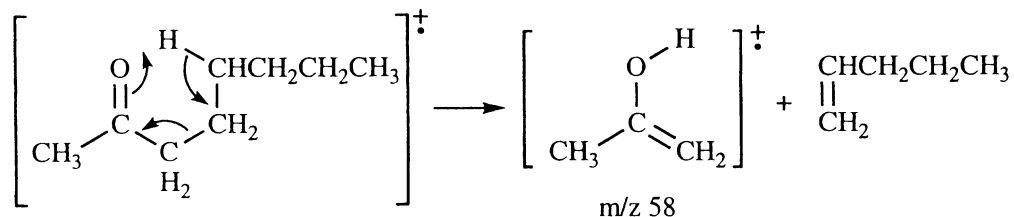
18-3 A compound has to have a hydrogen on a γ carbon (or other atom) in order for the McLafferty rearrangement to occur. Butan-2-one has no γ -hydrogen.



18-4



McLafferty rearrangement



18-5

The first value is the π to π^* ; the second value is the n to π^* . The values are approximate.

(a) < 200 nm; 280 nm; this simple ketone should have values similar to acetone

(b) 230 nm; 310 nm; conjugated system (210) plus 2 alkyl groups (20) = 230; the value of 310 nm is similar to Figure 18-7: ketone (280 nm base value) plus 30 nm for the conjugated double bond = 310 nm

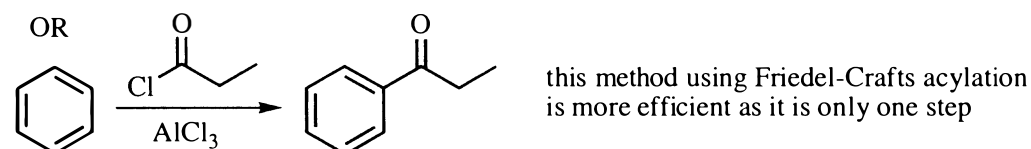
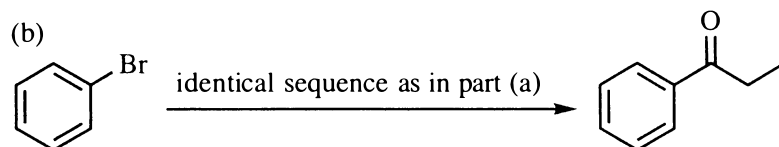
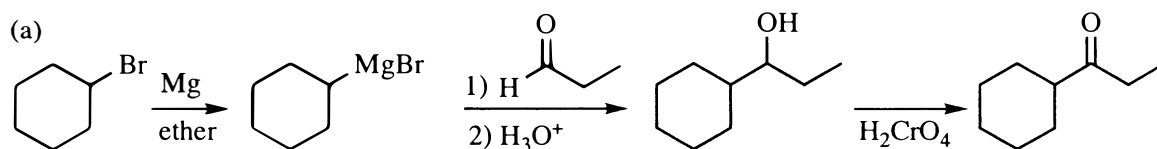
(c) 280 nm; 360 nm; conjugated system (210) plus 1 extra double bond (30) plus 4 alkyl groups (40) = 280; similar reasoning for the other transition, starting with an average base value of 290

(d) 270 nm; 350 nm; same as in (c) except only 3 alkyl groups instead of 4

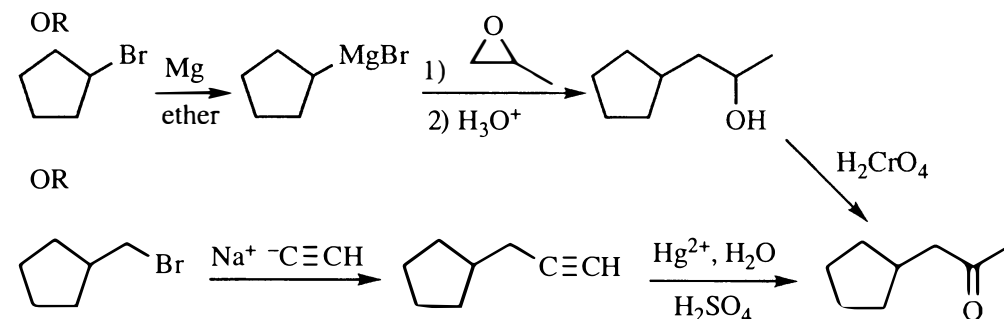
REMINDERS ABOUT SYNTHESIS PROBLEMS:

1. There may be more than one legitimate approach to a synthesis, especially as the list of reactions gets longer.
2. Begin your analysis by comparing the target to the starting material. If the product has more carbons than the reactant, you will need to use one of the small number of reactions that form carbon-carbon bonds.
3. Where possible, work backwards from the target back to the starting material.
4. **KNOW THE REACTIONS.** There is no better test of whether you know the reactions than attempting synthesis problems.

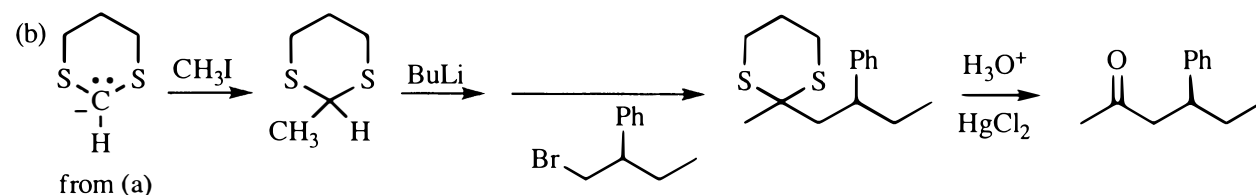
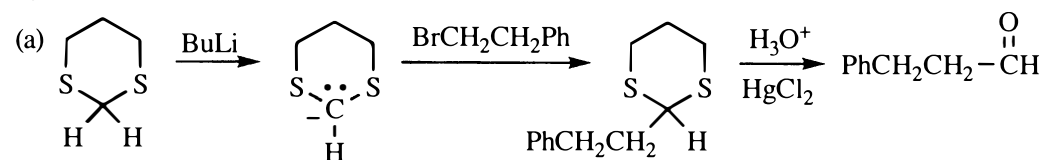
18-6 All three target molecules in this problem have more than six carbons, so all answers will include carbon-carbon-bond-forming reactions. So far, there are three types of reactions that form carbon-carbon bonds: the Grignard reaction, S_N2 substitution by an acetylide ion, and the Friedel-Crafts reactions (alkylation and acylation) on benzene.



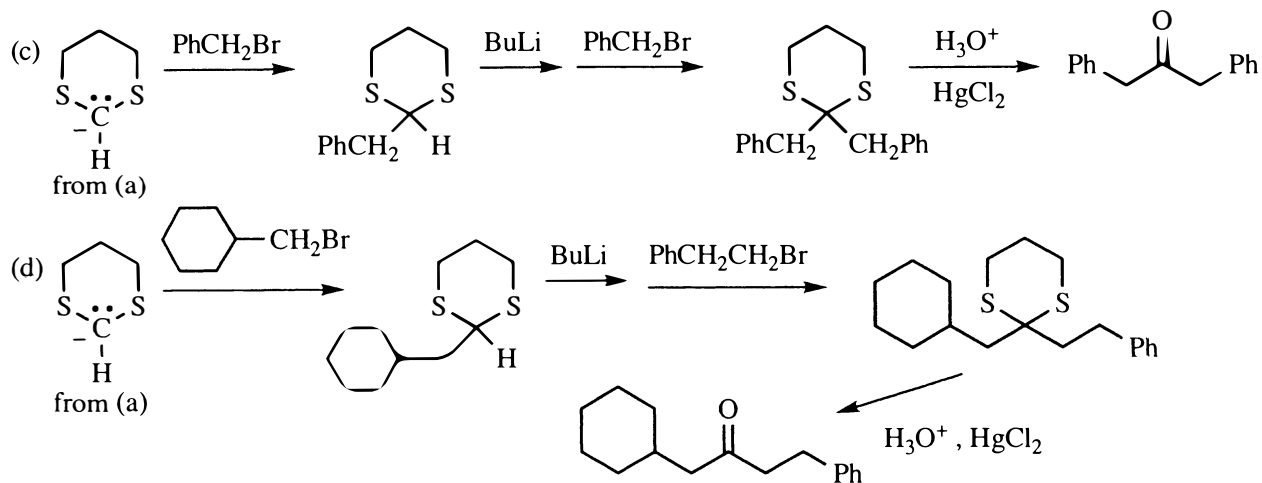
(c) a synthesis as in part (a) could also be used here



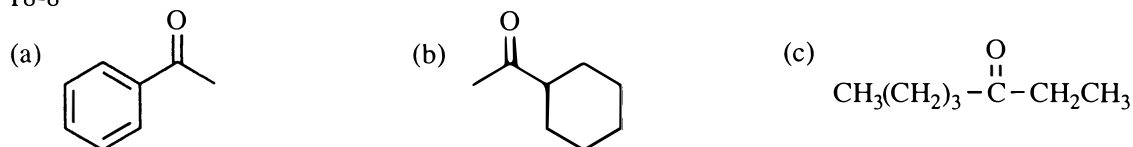
18-7



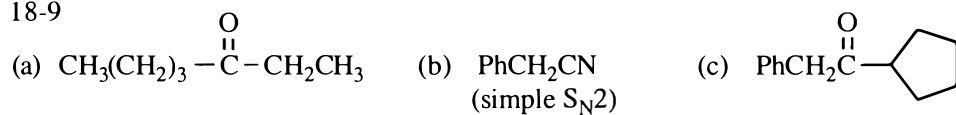
18-7 continued



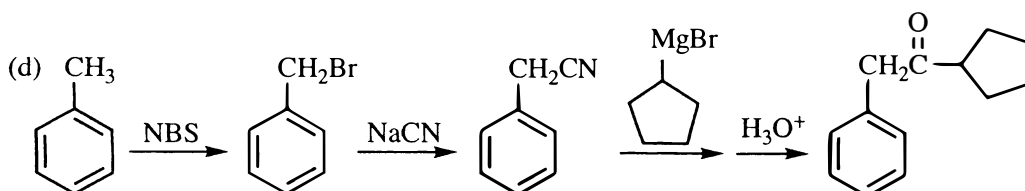
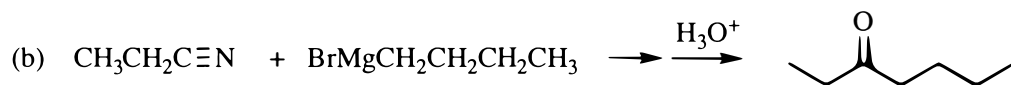
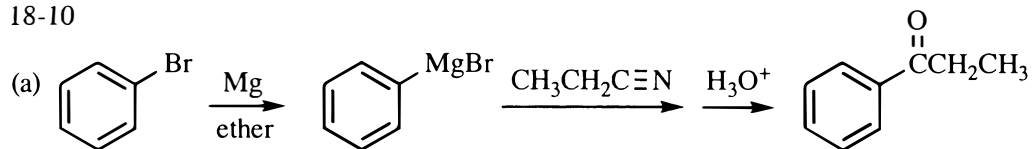
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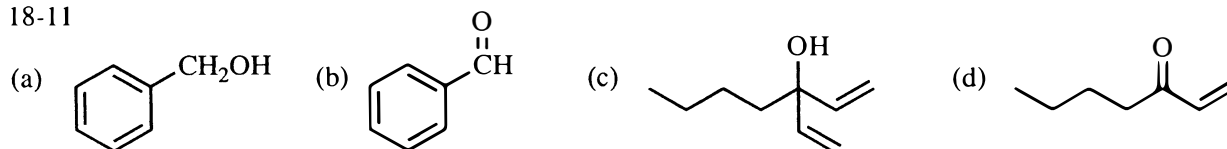
18-9



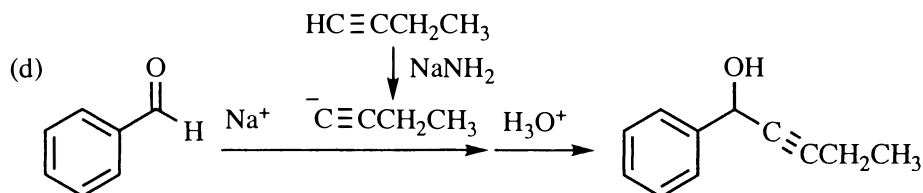
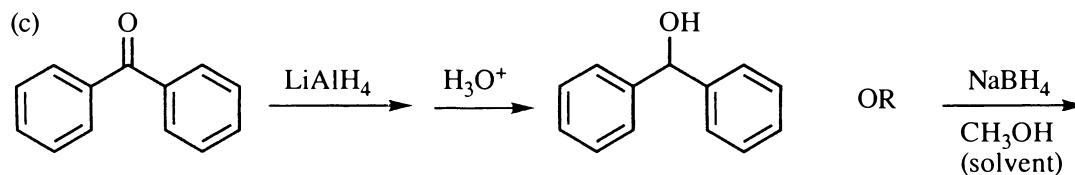
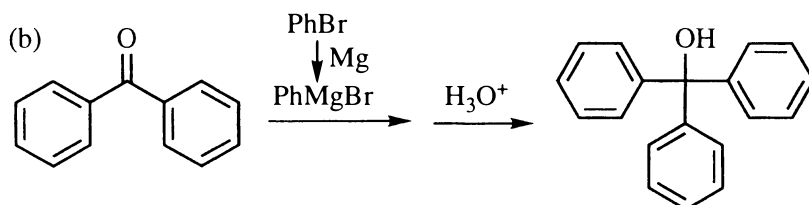
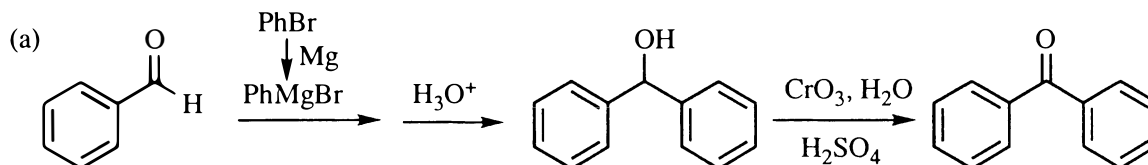
18-10



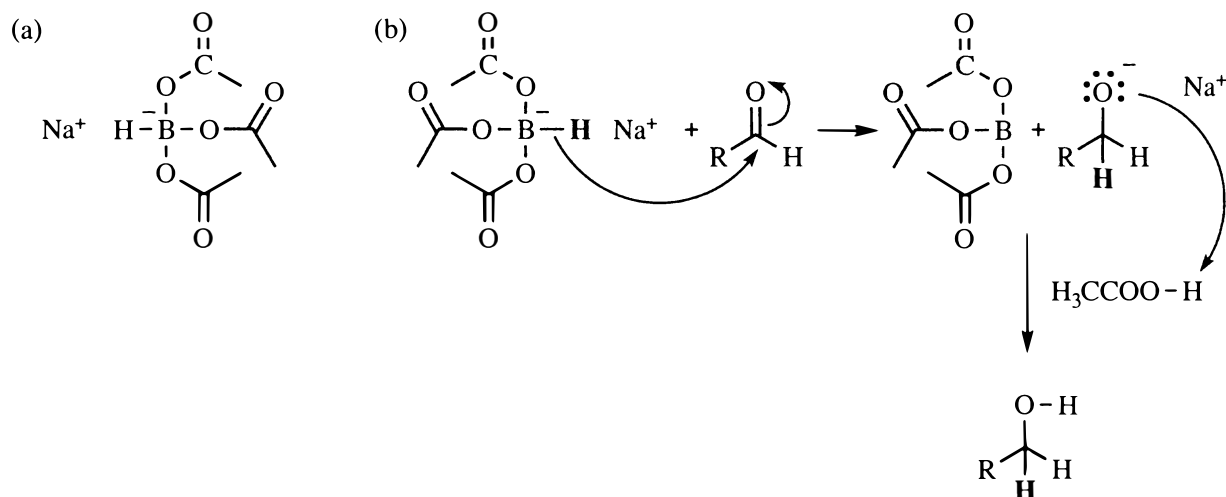
18-11



18-12 Review the reminders on p. 402. There are often more than one correct way to do syntheses, but a more direct route with fewer steps is usually better.

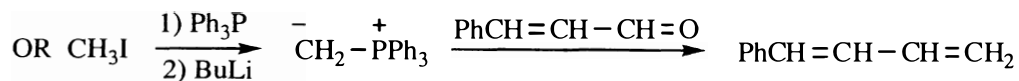
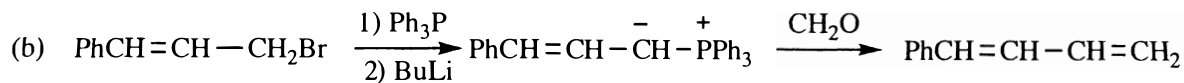
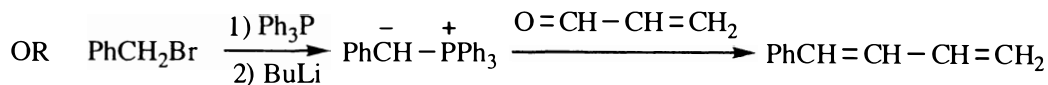
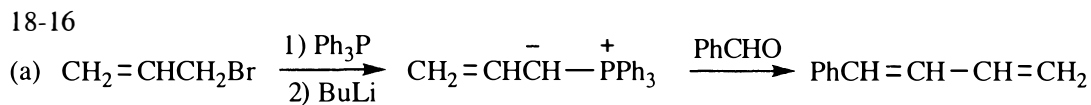
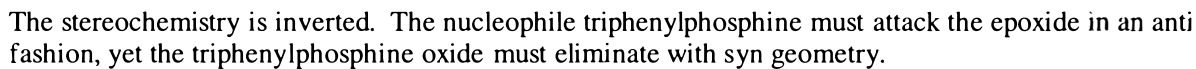


18-13 The triacetoxyborohydride ion is similar to borohydride, BH_4^- , where three acetoxy groups have replaced three hydrides.

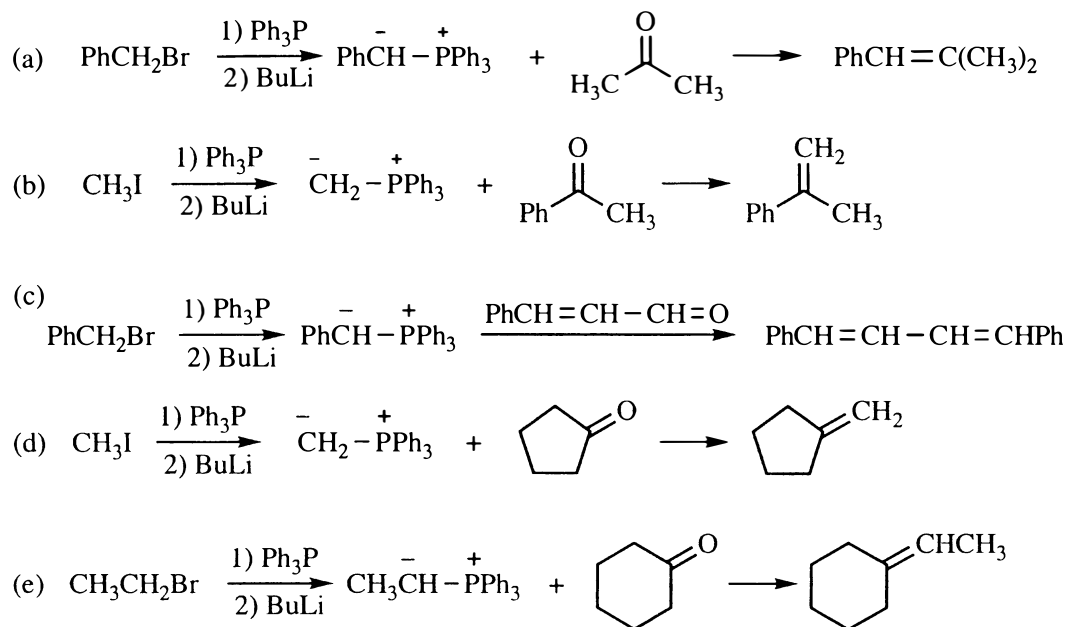


$$\text{CH}_3-\overset{\text{CH}_3}{\underset{\text{CH}_3}{\overset{+}{\text{P}}}}-\text{CH}_2\text{R} \xrightarrow{\text{BuLi}} \underset{\text{CH}_3}{\underset{\text{CH}_3}{\overset{+}{\text{P}}}}-\overset{-}{\text{C}}\text{HR} + \overset{-}{\text{C}}\text{H}_2-\overset{\text{CH}_3}{\underset{\text{CH}_3}{\overset{+}{\text{P}}}}-\text{CH}_2\text{R}$$

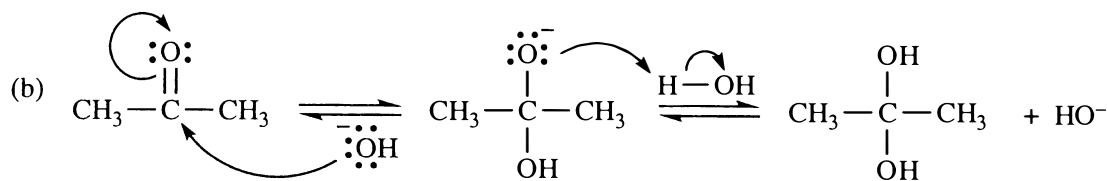
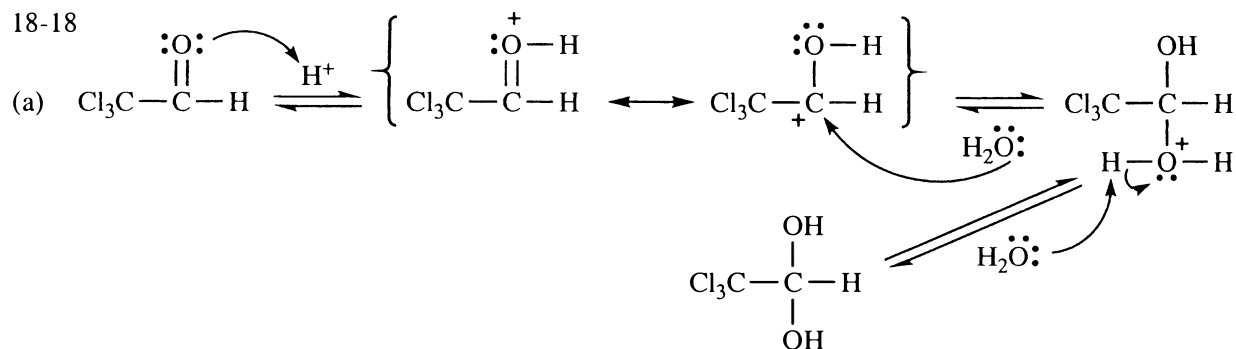
desired ylide wrong ylide



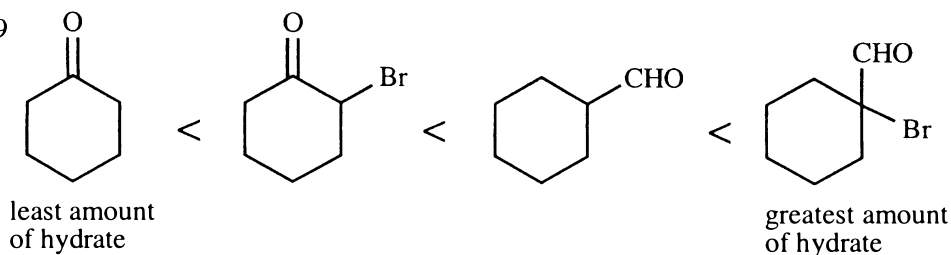
18-17 Many alkenes can be synthesized by two different Wittig reactions (as in the previous problem). The ones shown here form the phosphonium salt from the less hindered alkyl halide.



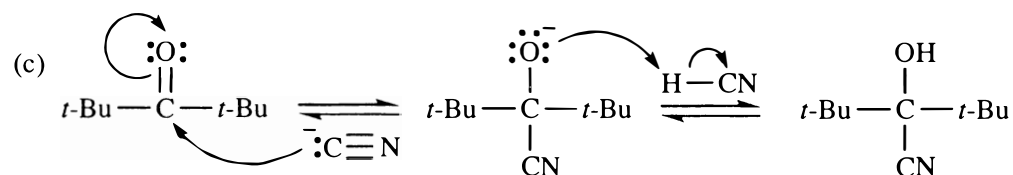
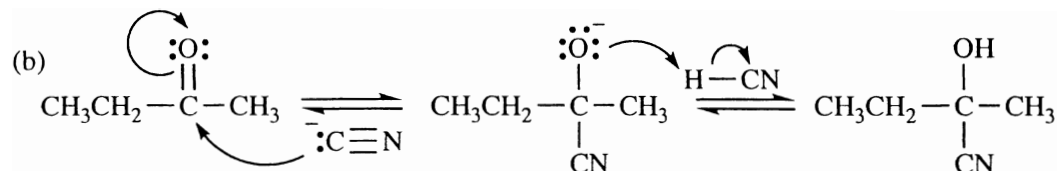
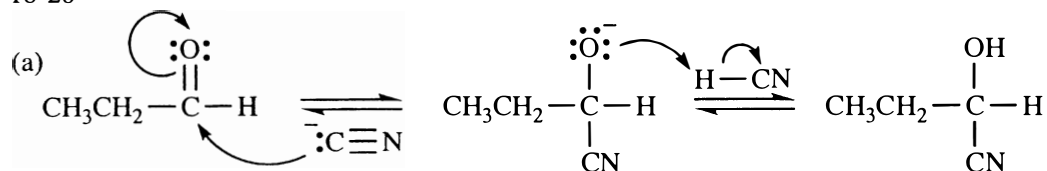
18-18



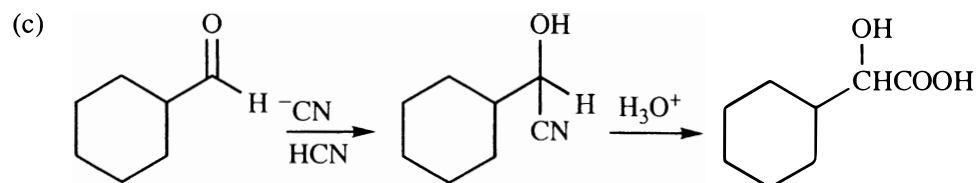
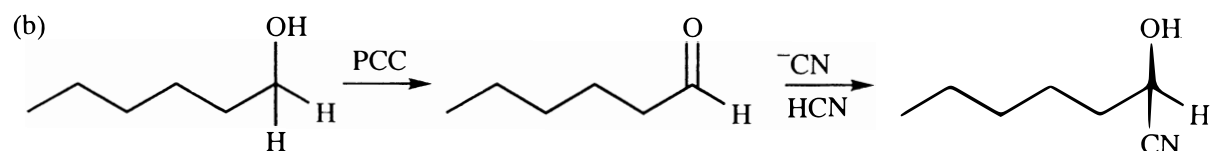
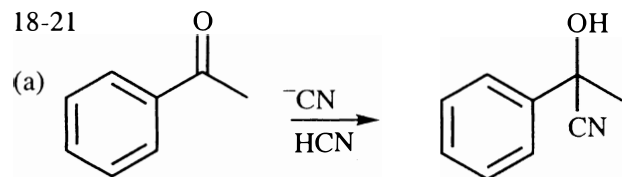
18-19



18-20



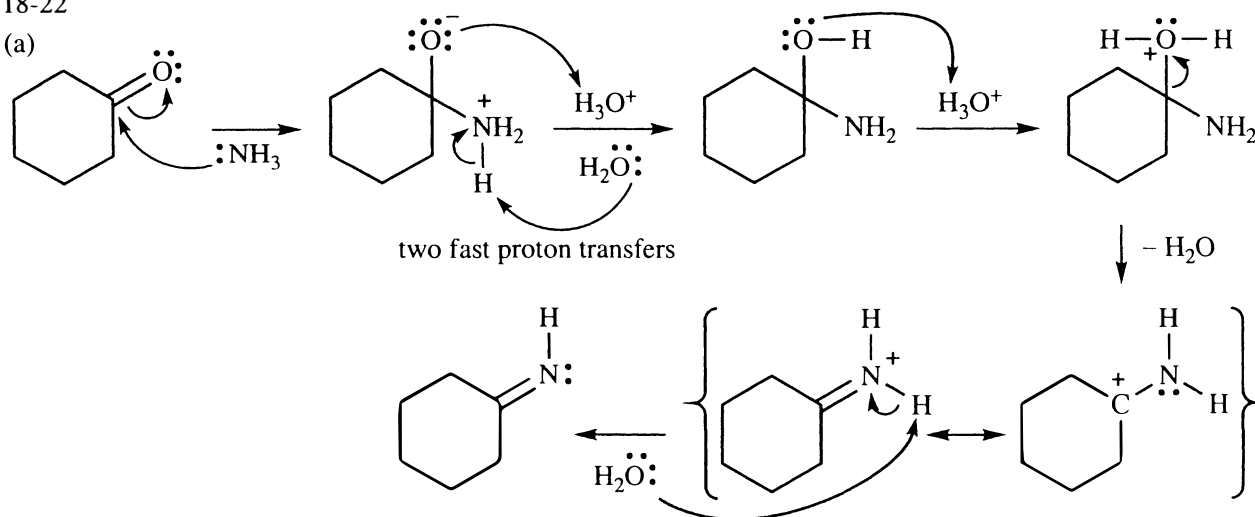
18-21



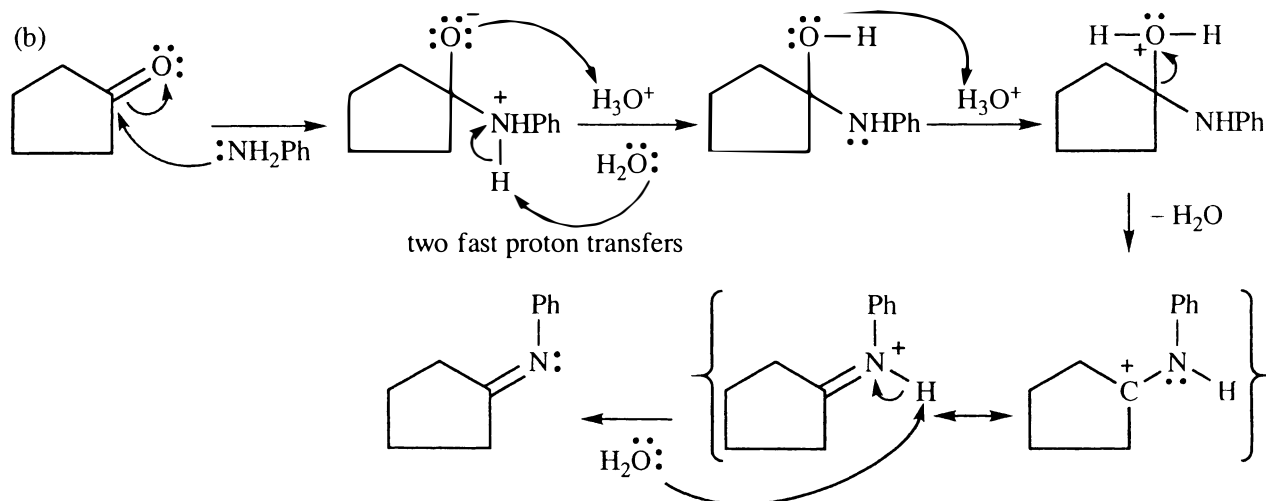
Note: Mechanisms of nucleophilic attack at carbonyl carbon frequently include species with both positive and negative charges. These species are very short-lived as each charge is quickly neutralized by a rapid proton transfer; in fact, these steps are the fastest of the whole mechanism. In most cases, this Solutions Manual will show these *two* steps as occurring at the same time, even though you have been admonished to show *all* steps of a mechanism separately. The practice of showing these proton transfers in one step is legitimate as long as it is understood that these are *two* fast steps.

18-22

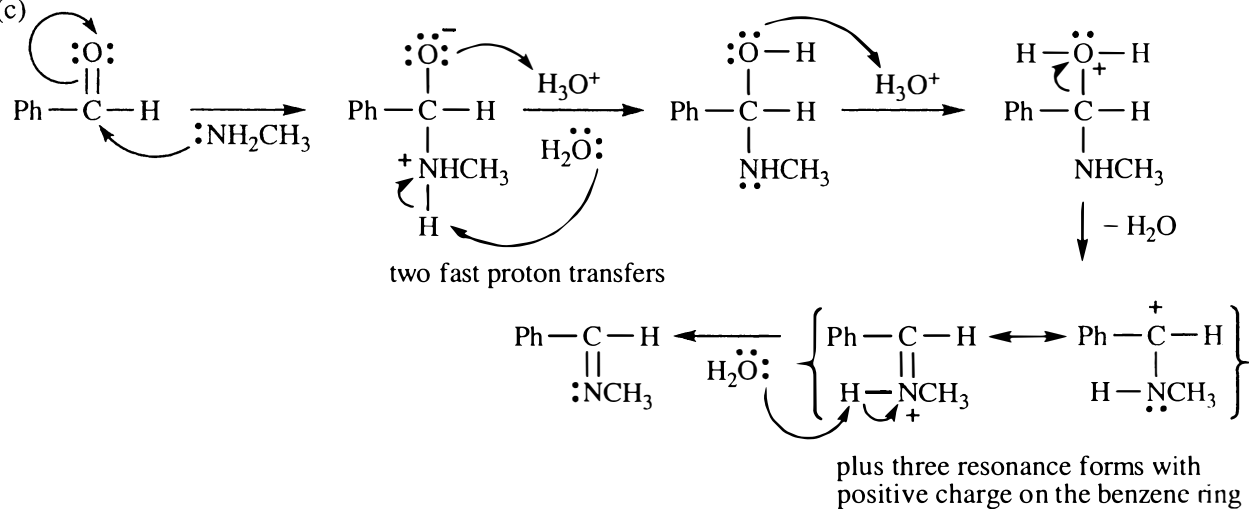
(a)



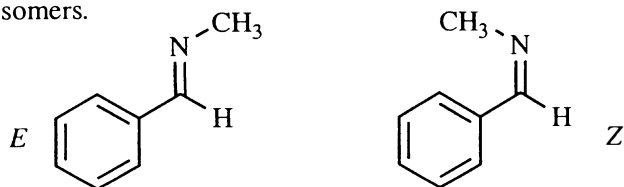
(b)



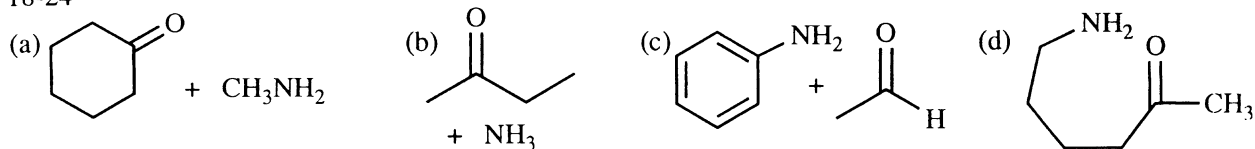
(c)



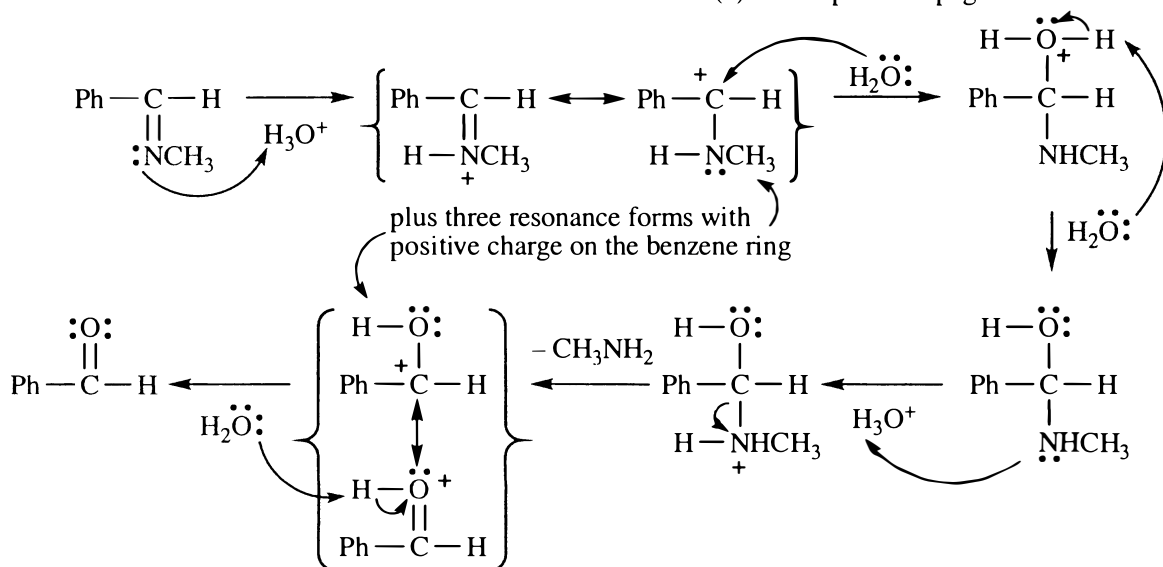
18-23 Whenever a double bond is formed, stereochemistry must be considered. The two compounds are the *Z* and *E* isomers.



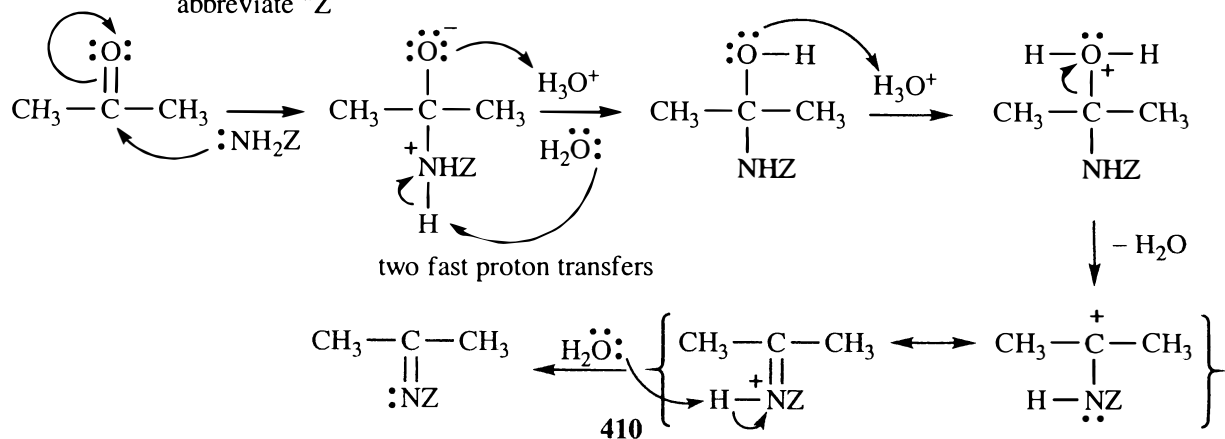
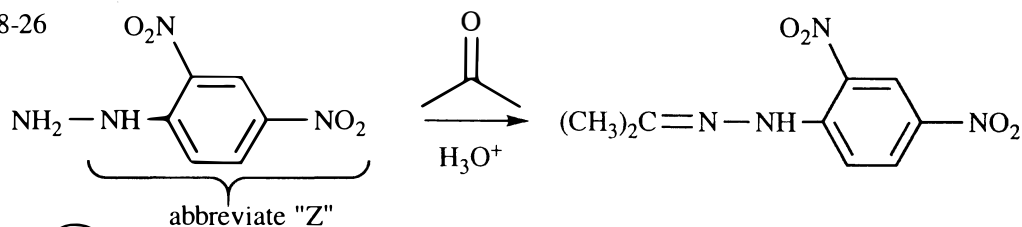
18-24

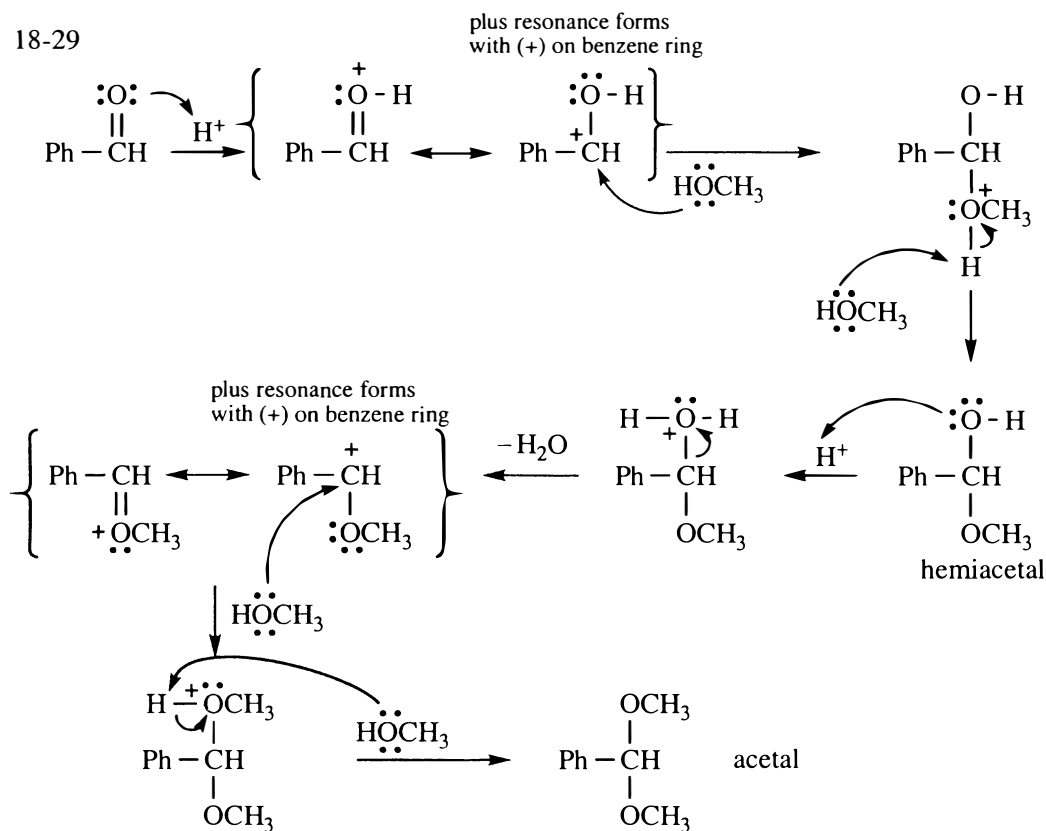
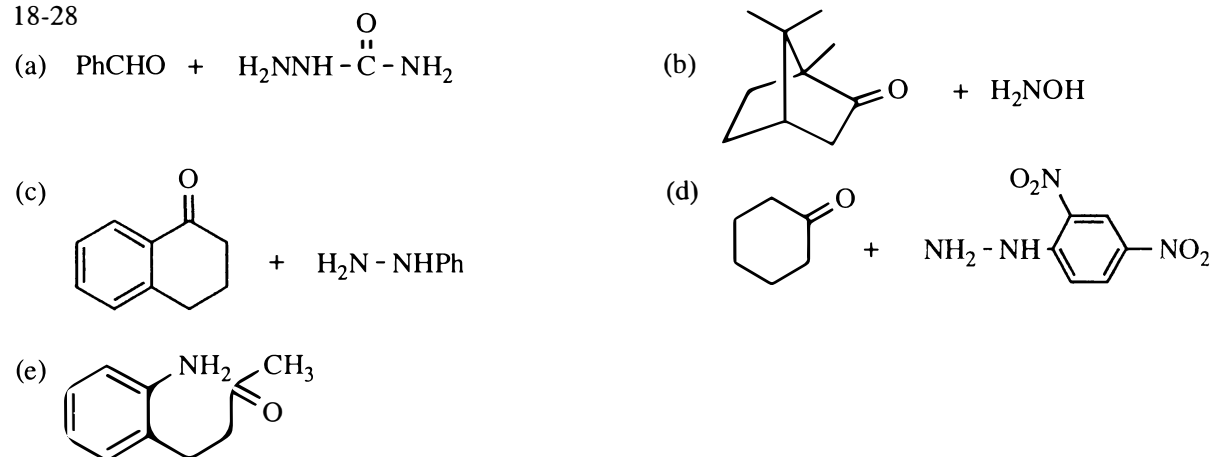
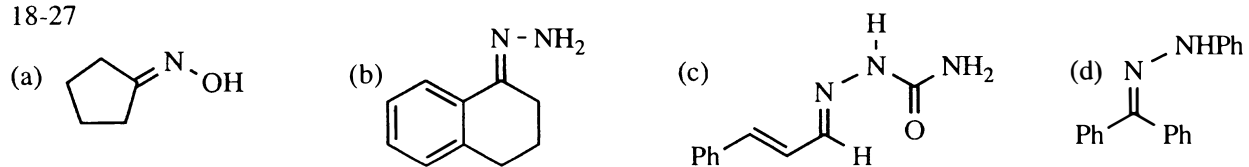


18-25 This mechanism is the reverse of the one shown in 18-22(c) on the previous page.

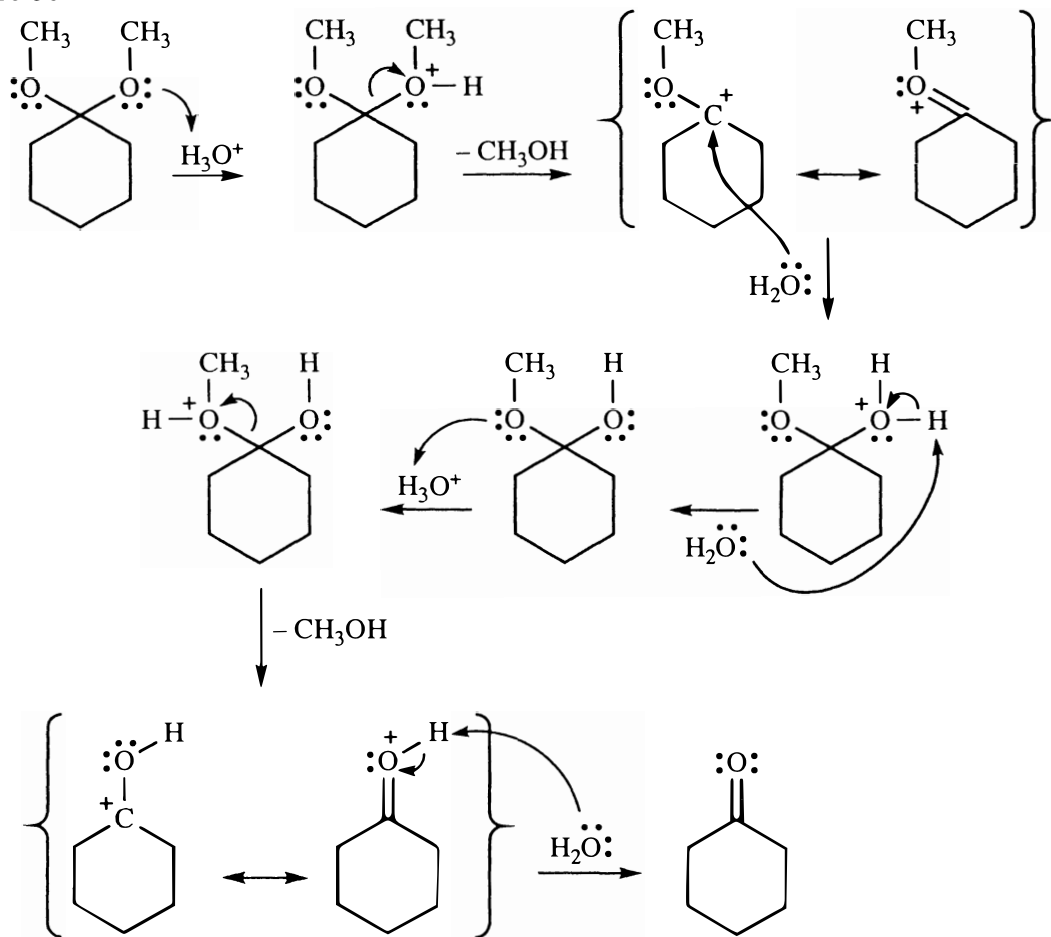


18-26

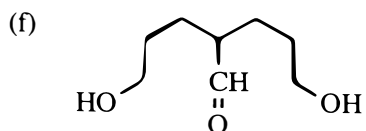
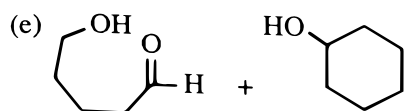
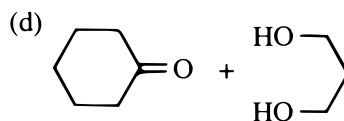
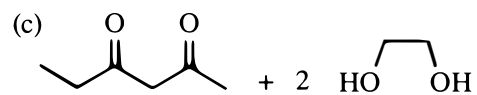
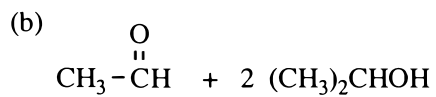
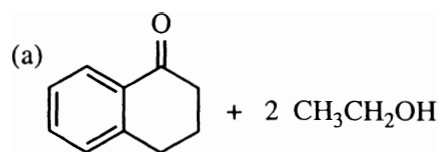


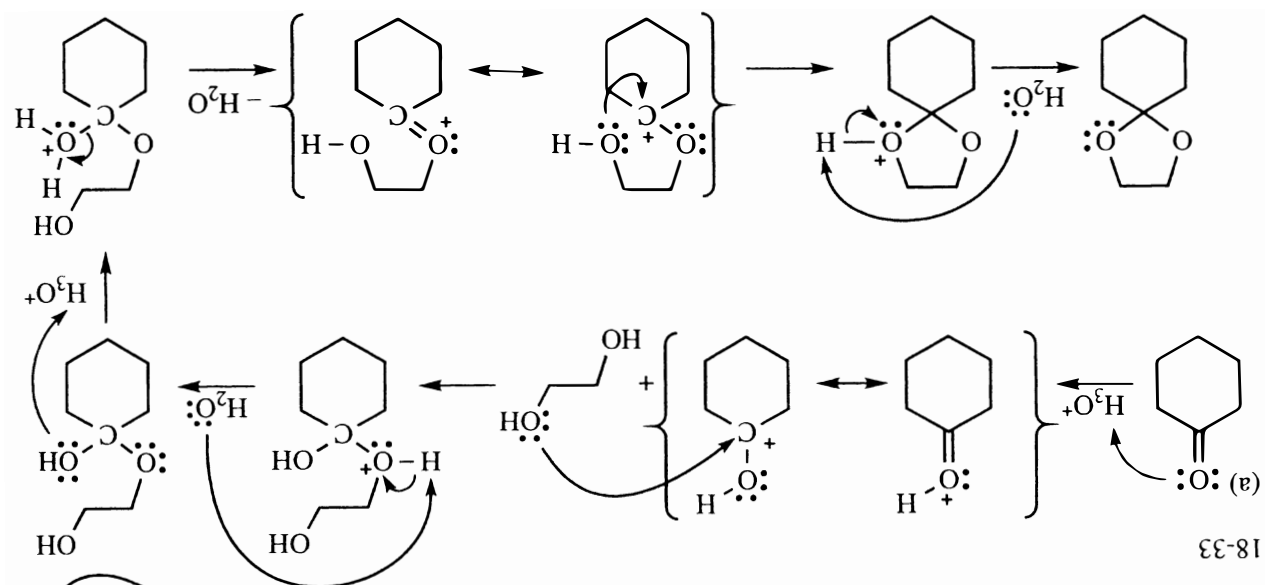
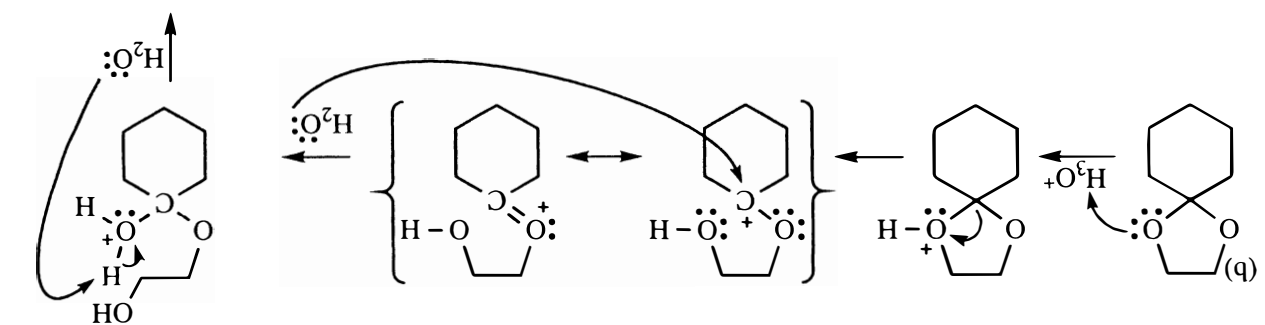


18-30

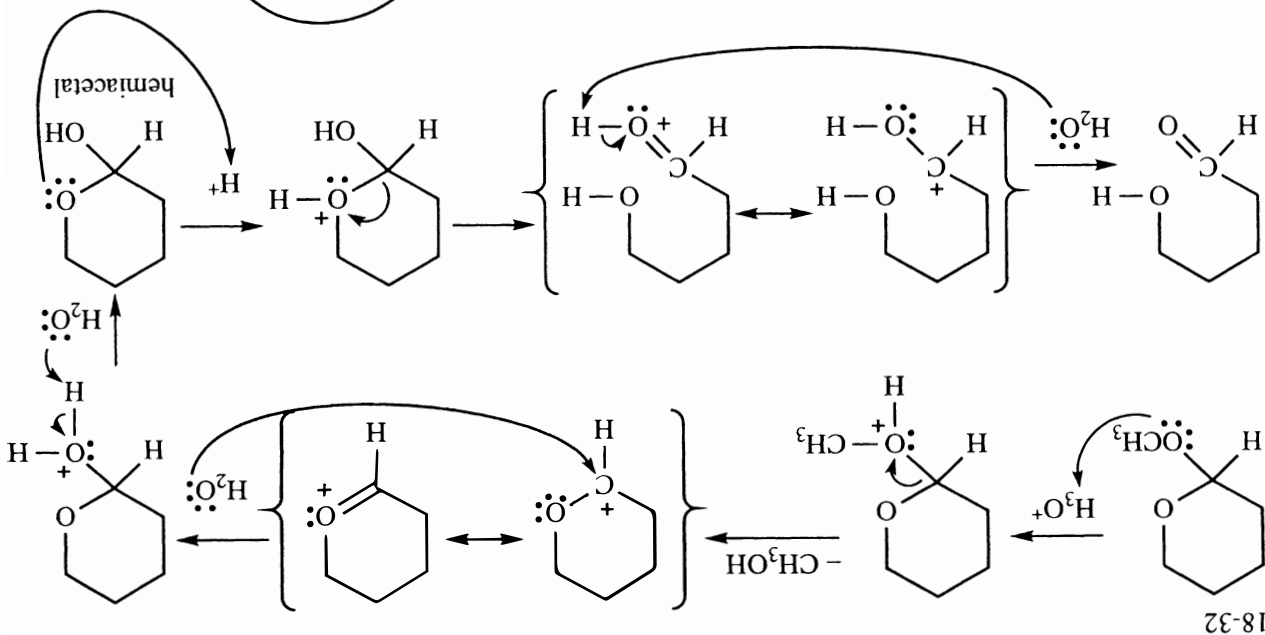


18-31



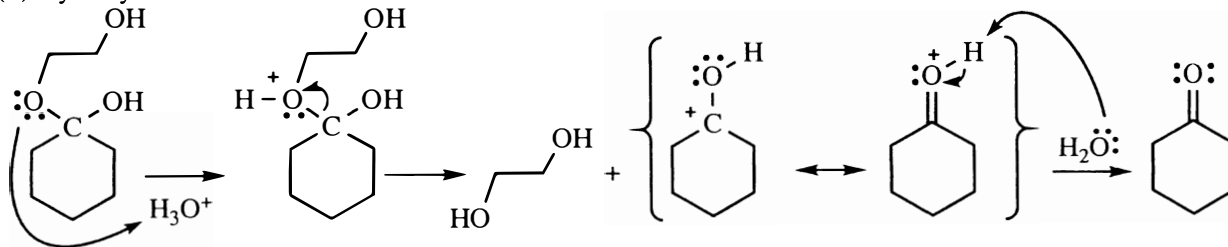


18-33

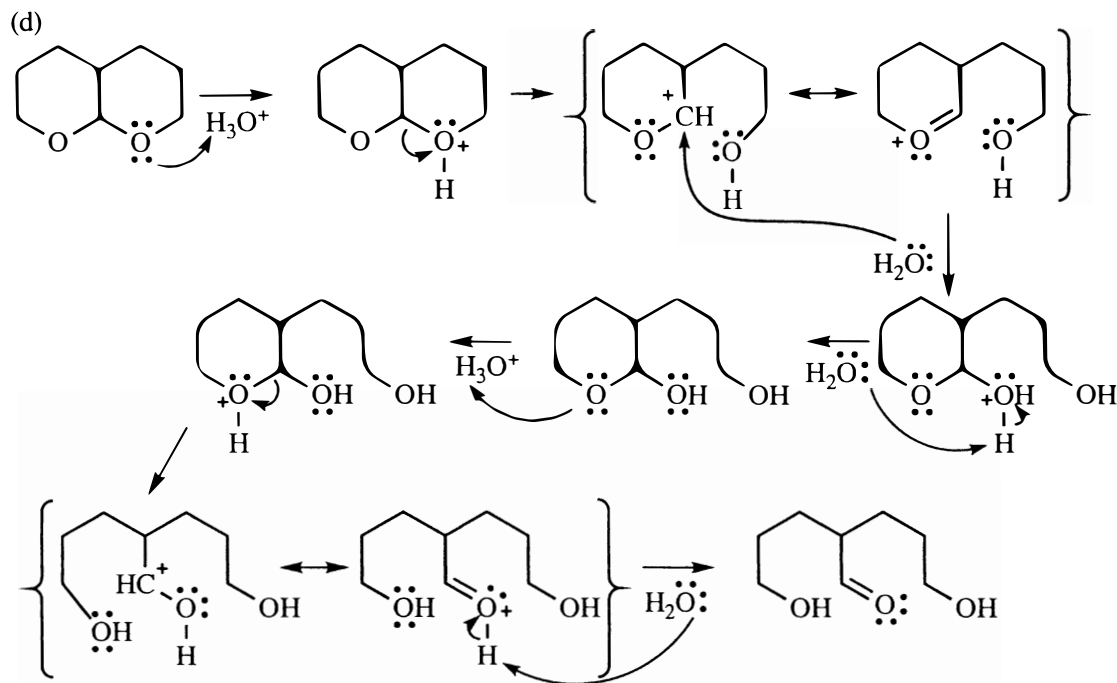


18-33 continued

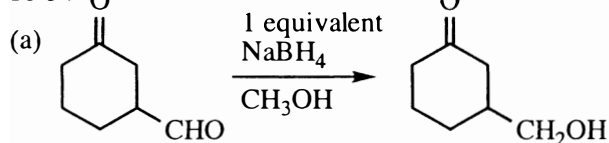
(b) hydrolysis mechanism continued



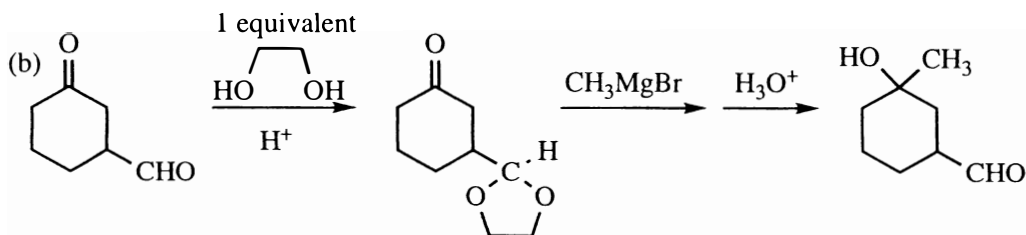
(c) The mechanisms of formation of an acetal and hydrolysis of an acetal are identical, just the reverse order. This has to be true because this process is an equilibrium: if the forward steps follow a minimum energy path, then the reverse steps have to follow the identical minimum energy path. This is the famous Principle of Microscopic Reversibility, text section 8-4A.



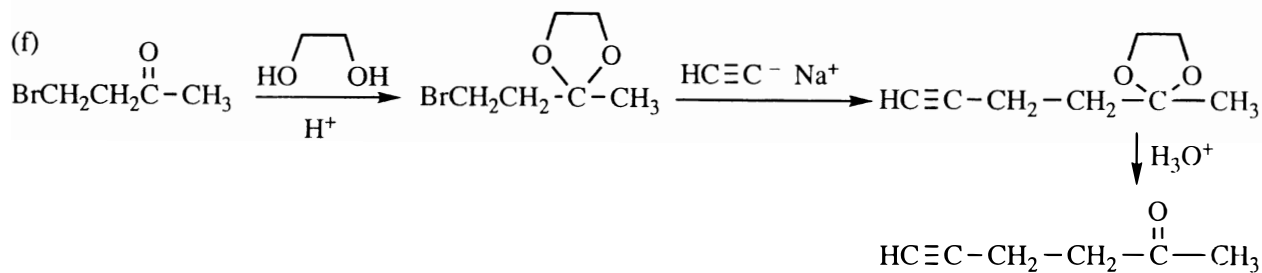
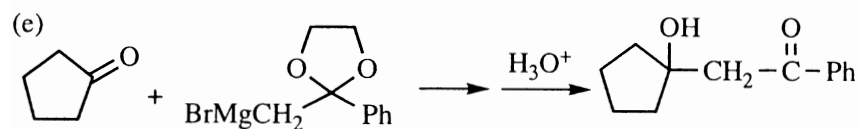
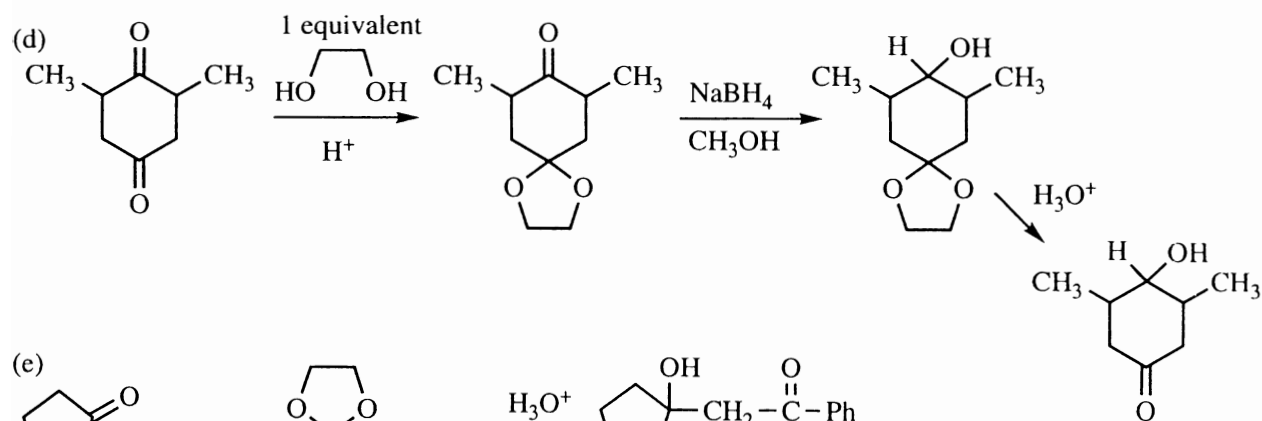
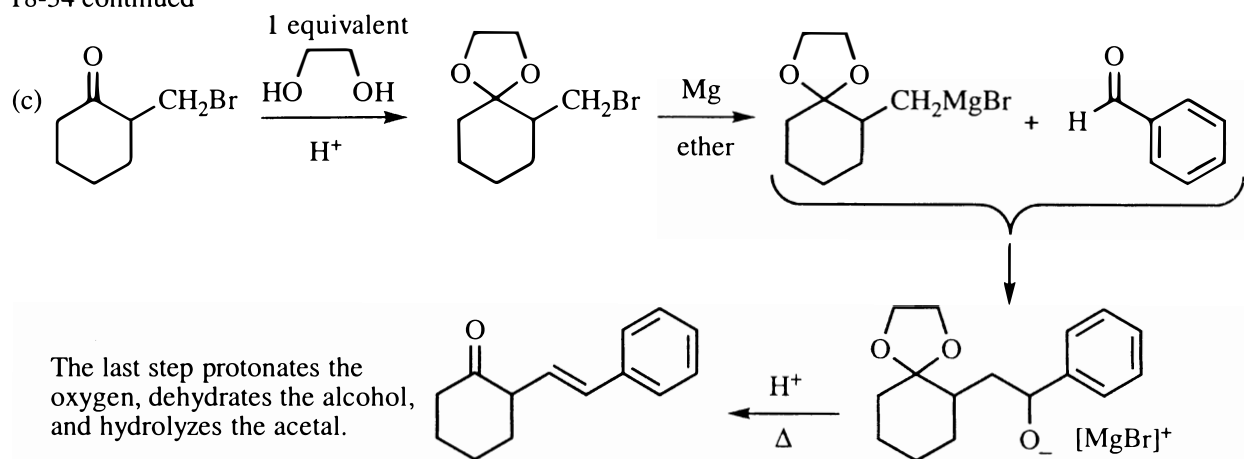
18-34



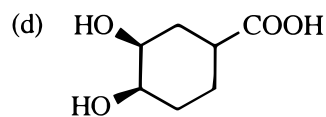
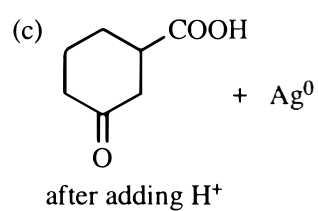
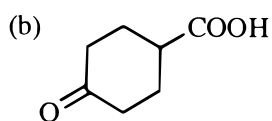
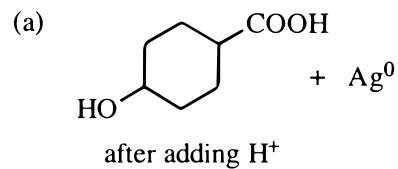
Aldehydes are reduced faster than ketones (keeping this reaction cold will increase selectivity). Alternatively, sodium triacetoxyborohydride could be used for this reduction; see problem 18-13.



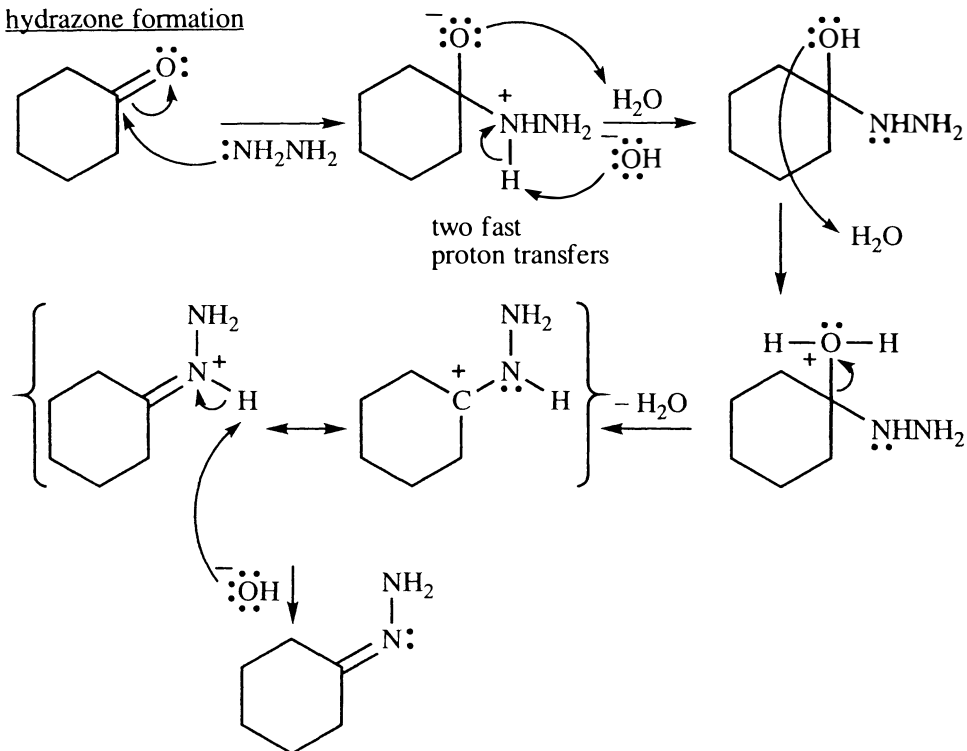
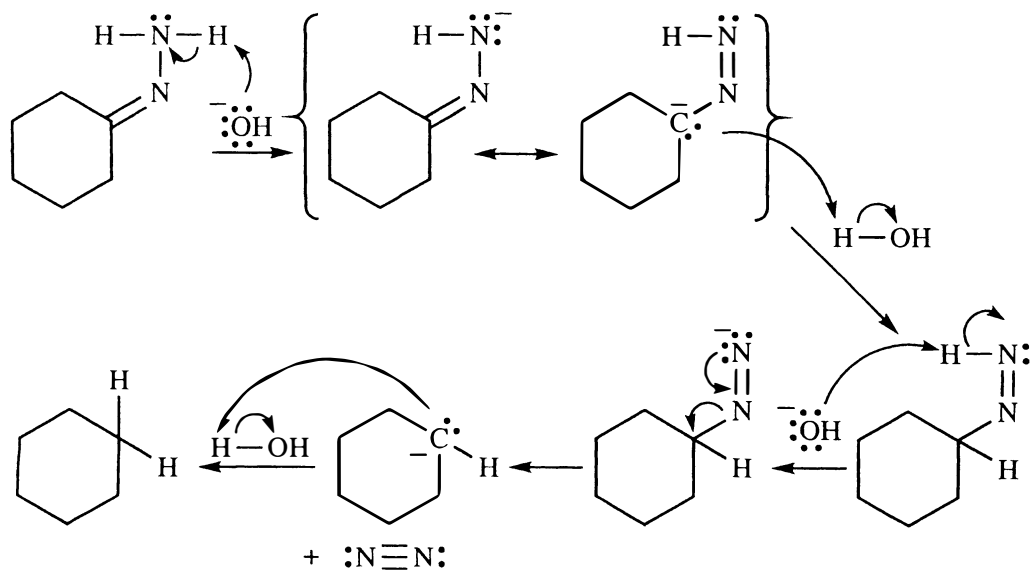
18-34 continued



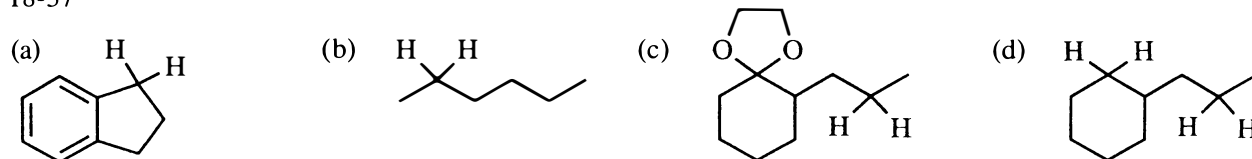
18-35



18-36

hydrazone formationreduction of the hydrazone

18-37

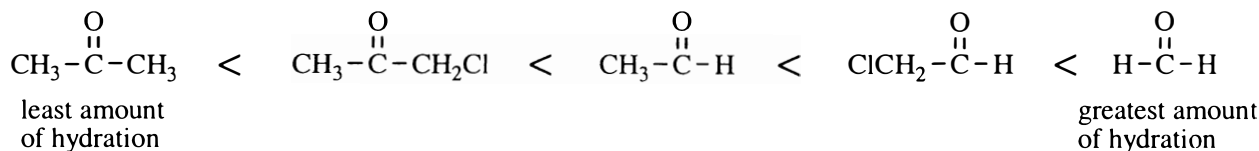


18-38 Please refer to solution 1-20, page 12 of this Solutions Manual.

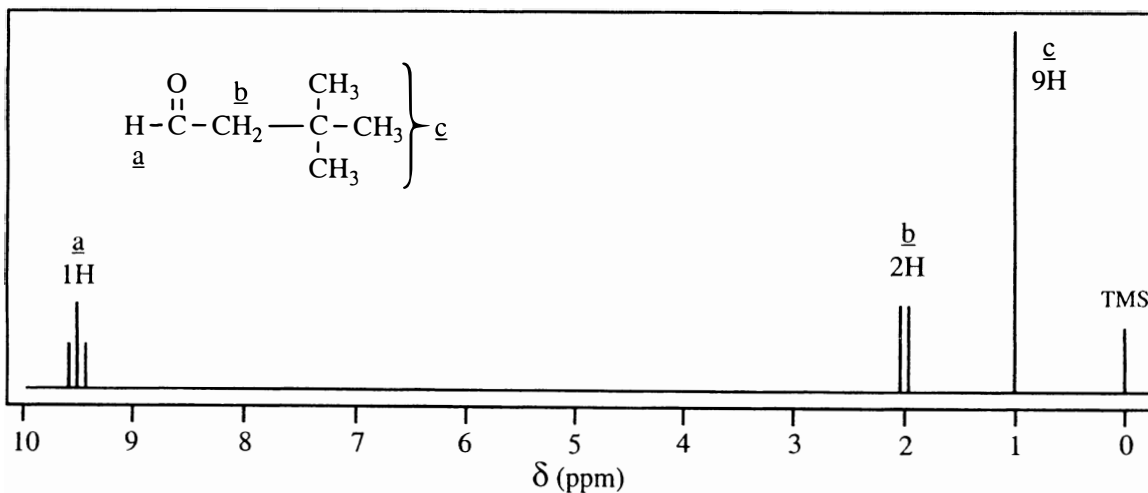
18-39 IUPAC names first; then common names. Please see the note on p. 136 of this Solutions Manual regarding placement of position numbers.

- | | |
|--|--|
| (a) heptan-2-one; methyl <i>n</i> -pentyl ketone | (g) 4-bromo-2-methylhexanal; no common name |
| (b) heptan-4-one; di- <i>n</i> -propyl ketone | (h) 3-phenylprop-2-enal; cinnamaldehyde |
| (c) heptanal; no simple common name | (i) hexa-2,4-dienal; no common name |
| (d) benzophenone; diphenyl ketone | (j) 3-oxopentanal; no common name |
| (e) butanal; butyraldehyde | (k) 3-oxocyclopentanecarbaldehyde; no common name |
| (f) propanone; acetone (IUPAC accepts "acetone") | (l) <i>cis</i> -2,4-dimethylcyclopentanone; no common name |

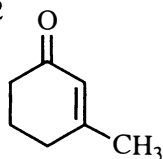
18-40 In order of increasing equilibrium constant for hydration:



18-41



18-42



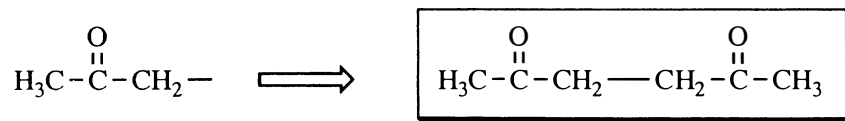
By comparison with similarly substituted molecules shown in the text:

$\pi \rightarrow \pi^*$ base value (210) plus 3 alkyl groups (30) = 240 nm
 $n \rightarrow \pi^*$ 300-320 nm

18-43

$C_6H_{10}O_2$ indicates two elements of unsaturation.

The IR absorption at 1708 cm^{-1} suggests a ketone, or possibly two ketones since there are two oxygens and two elements of unsaturation. The NMR singlets in the ratio of 2 : 3 indicate a highly symmetric molecule. The singlet at δ 2.15 is probably methyl next to carbonyl, and the singlet at δ 2.67 integrating to two is likely to be CH_2 on the other side of the carbonyl.

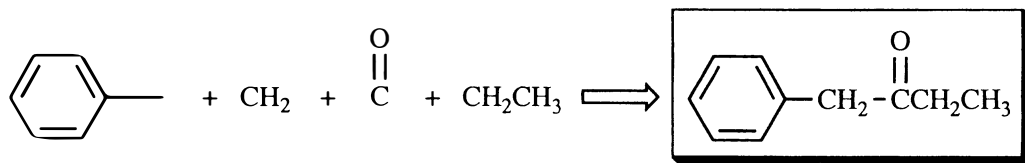


Since the molecular formula is double this fragment, the molecule must be twice the fragment.

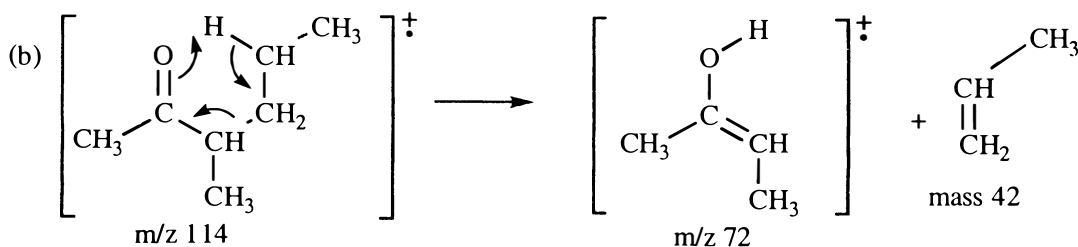
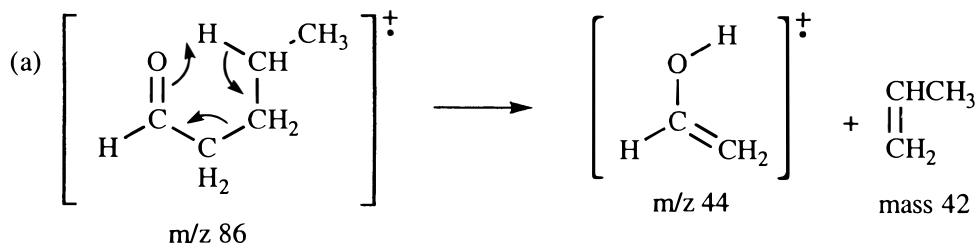
Two questions arise. Why is the integration 2 : 3 and not 4 : 6? Integration provides a *ratio*, not absolute numbers, of hydrogens. Why don't the two methylenes show splitting? Adjacent, *identical* hydrogens, with identical chemical shifts, do not split each other; the signals for ethane or cyclohexane appear as singlets.

18-44 The formula $C_{10}H_{12}O$ indicates 5 elements of unsaturation. A solid 2,4-DNP derivative suggests an aldehyde or a ketone, but a negative Tollens test precludes the possibility of an aldehyde; therefore, the unknown must be a ketone.

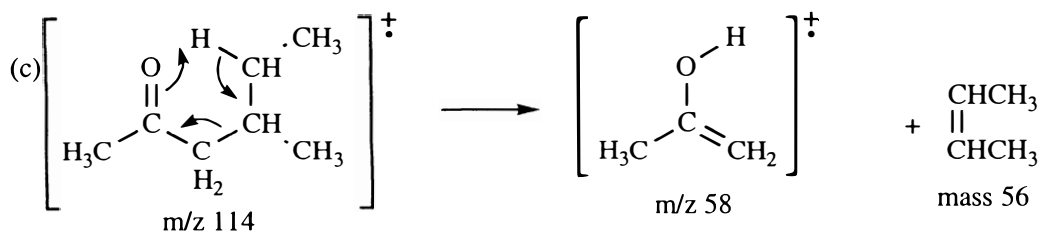
The NMR shows the typical ethyl pattern at δ 1.0 (3H, triplet) and δ 2.5 (2H, quartet), and a monosubstituted benzene at δ 7.3 (5H, multiplet). The singlet at δ 3.7 is a CH_2 , but quite far downfield, apparently deshielded by two groups. Assemble the pieces:



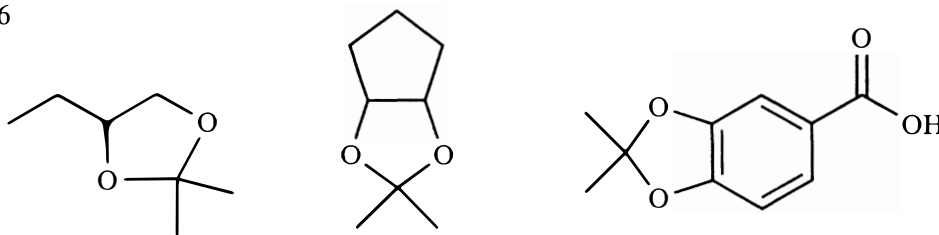
18-45



18-45 continued



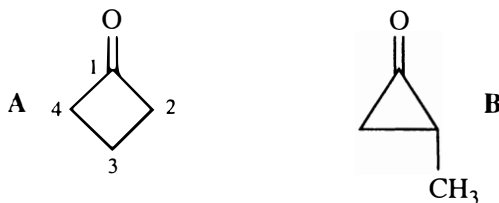
18-46



18-47

A molecular ion of m/z 70 means a fairly small molecule. A solid semicarbazone derivative and a negative Tollens test indicate a ketone. The carbonyl (CO) has mass 28, so $70 - 28 = 42$, enough mass for only 3 more carbons. The molecular formula is probably C_4H_6O (mass 70); with two elements of unsaturation, we can infer the presence of a double bond or a ring in addition to the carbonyl.

The IR shows a strong peak at 1790 cm^{-1} , indicative of a ketone in a small ring. No peak in the $1600\text{--}1650\text{ cm}^{-1}$ region shows the absence of an alkene. The only possibilities for a small ring ketone containing four carbons are these:



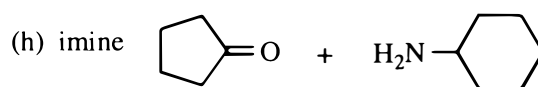
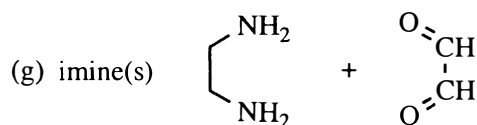
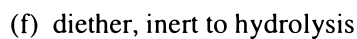
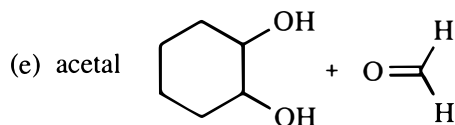
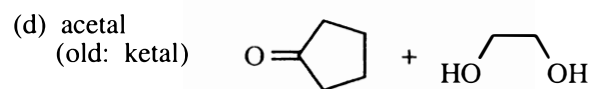
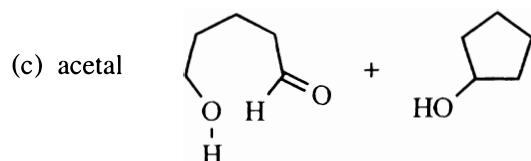
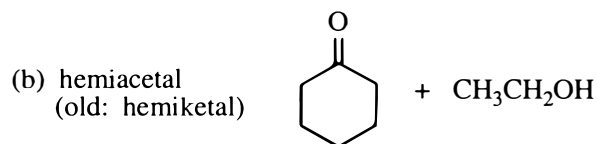
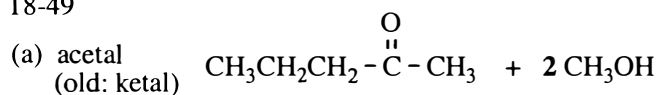
The HNMR can distinguish these. No methyl doublet appears in the NMR spectrum, ruling out **B**. The NMR does show a 4H triplet at δ 3.1; this signal comes from the two methylenes (C-2 and C-4) adjacent to the carbonyl, split by the two hydrogens on C-3. The signal for the methylene at C-3 appears at δ 2.0, roughly a quintet because of splitting by four neighboring protons.

The unknown is cyclobutanone, **A**. The symmetry indicated by the carbon NMR rules out structure **B**. The IR absorption of the carbonyl at 1790 cm^{-1} is characteristic of small ring ketones; ring strain strengthens the carbon-oxygen double bond, increasing its frequency of vibration. (See Section 12-9 in the text.)

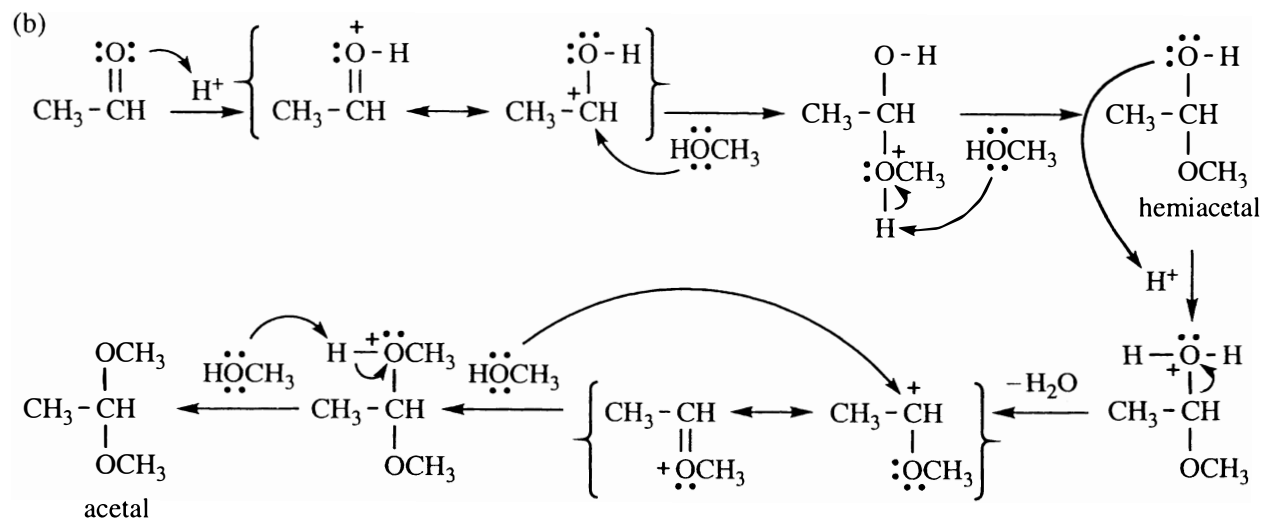
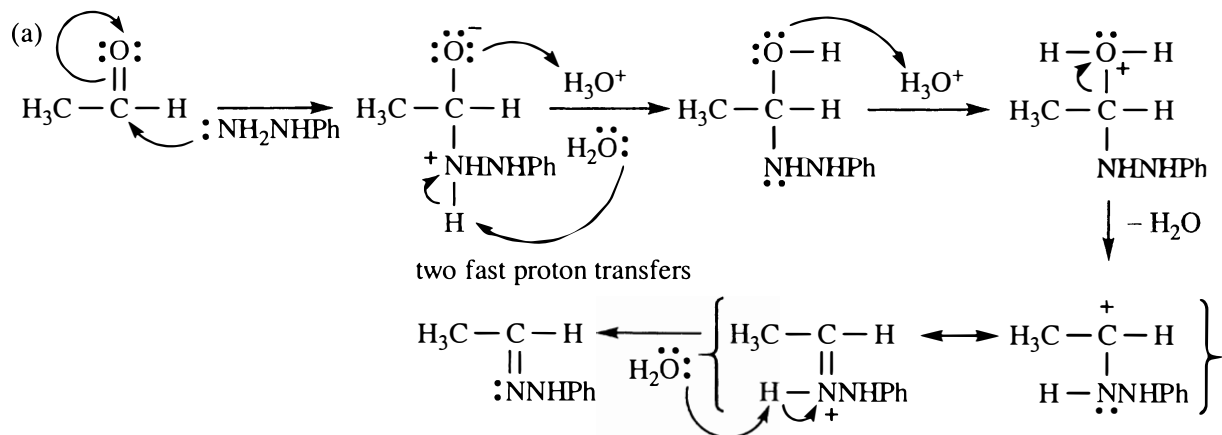
18-48

- (a) The conjugated diene has a maximum at 235 nm (see Solved Problem 15-3) and the ketone has a maximum at about 237 nm, so the π to π^* transition cannot be used to differentiate the compounds.
 (b) The ketone has an n to π^* transition around 315 nm that the diene cannot have.

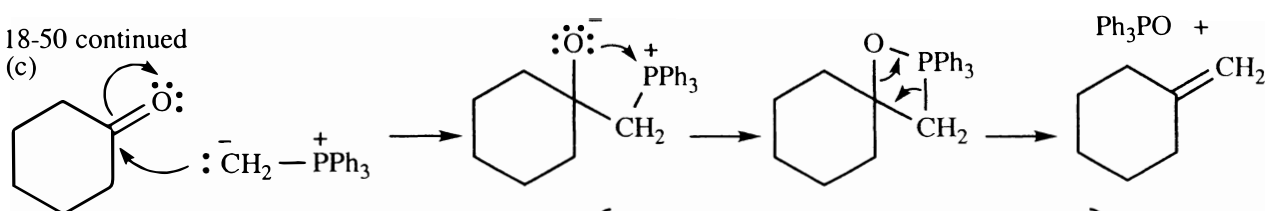
18-49



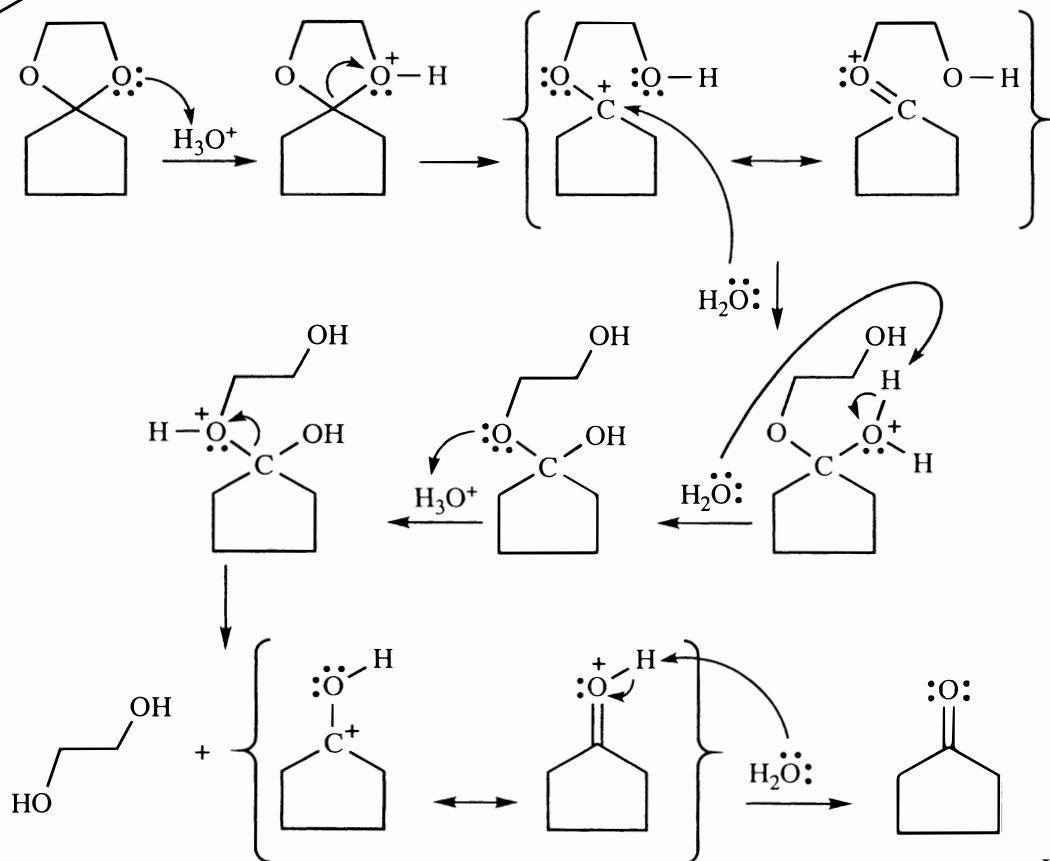
18-50



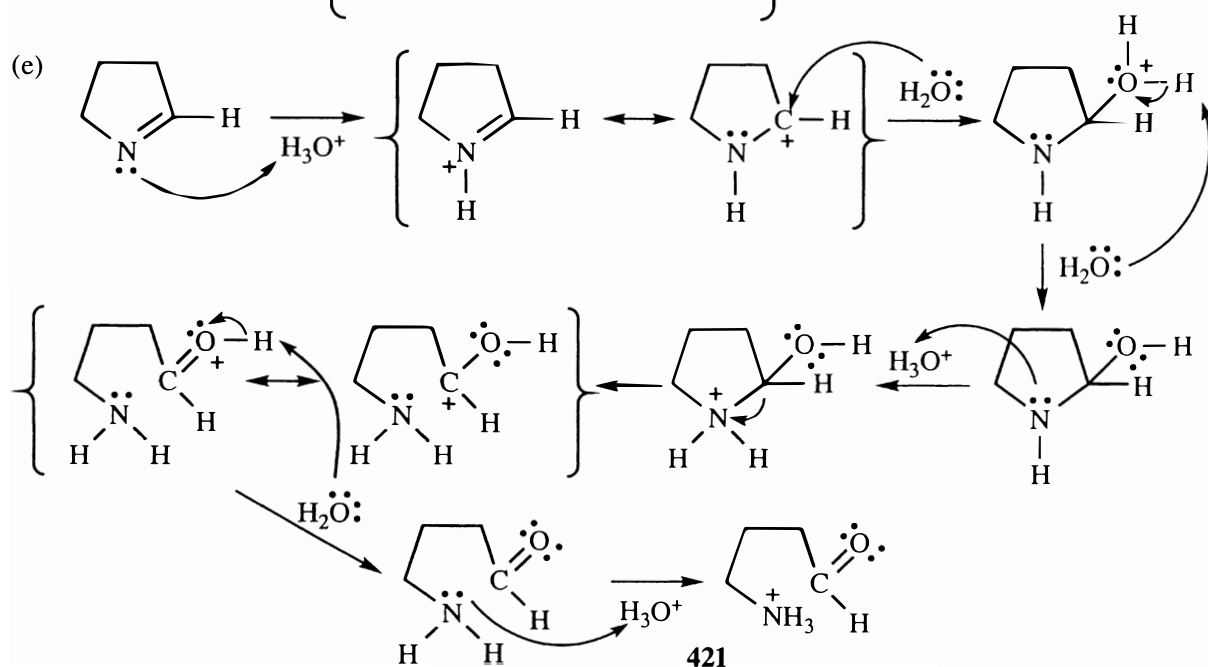
18-50 continued
(c)



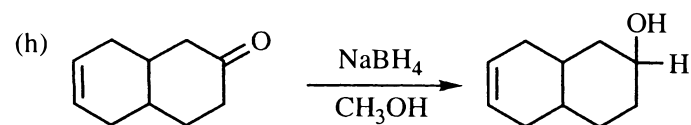
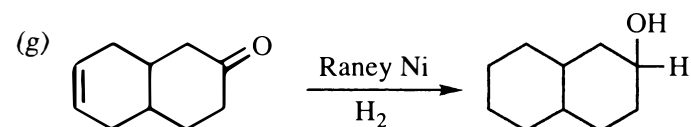
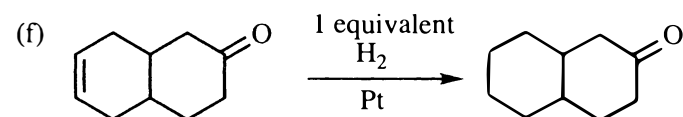
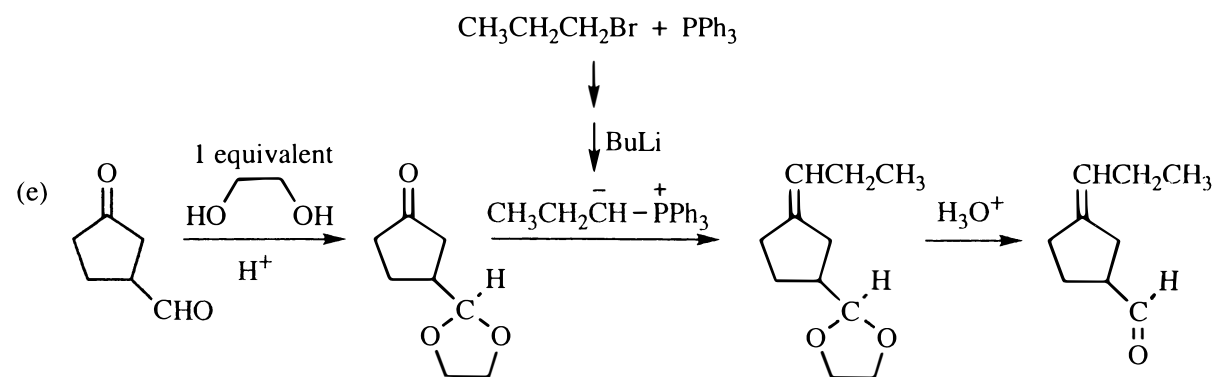
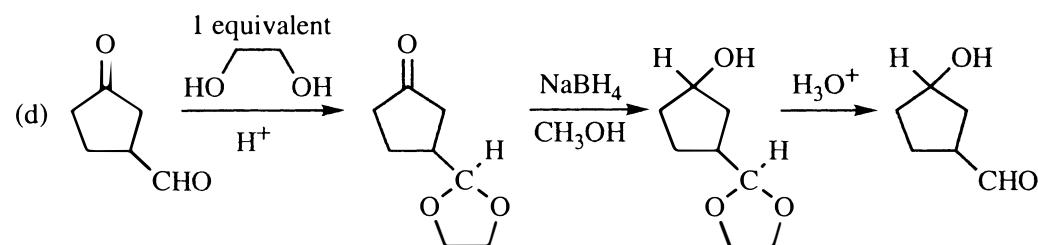
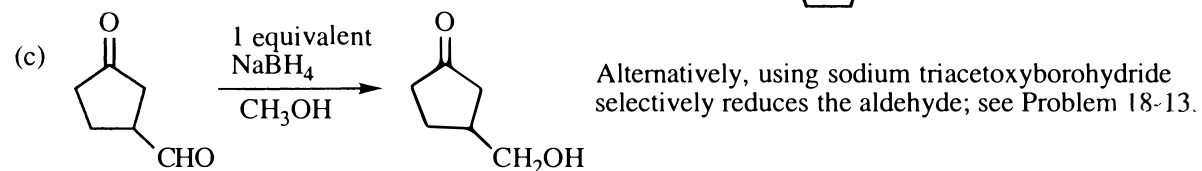
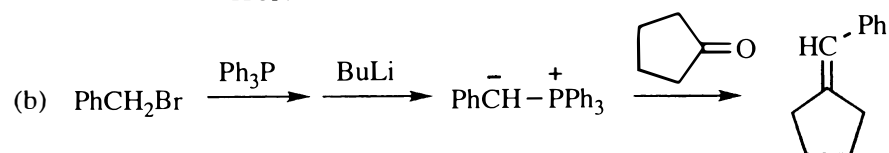
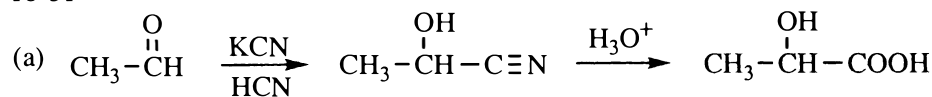
(d)



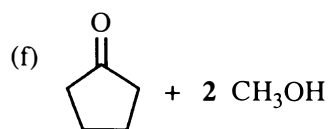
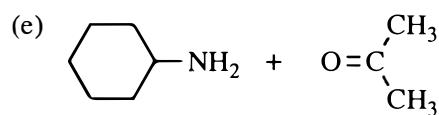
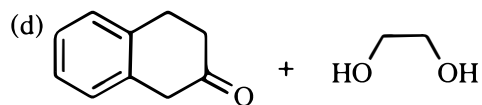
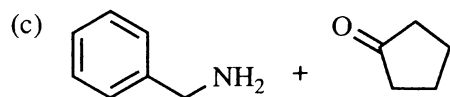
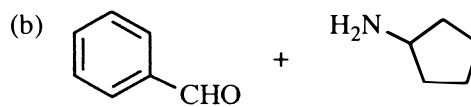
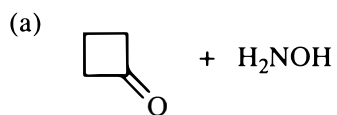
(e)



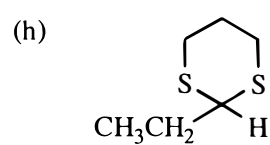
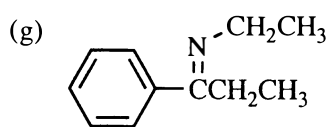
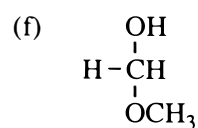
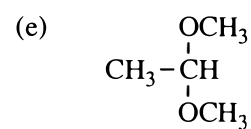
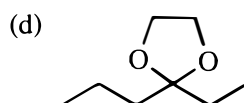
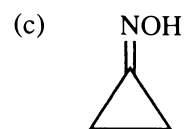
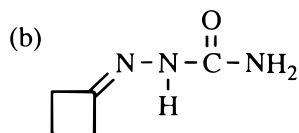
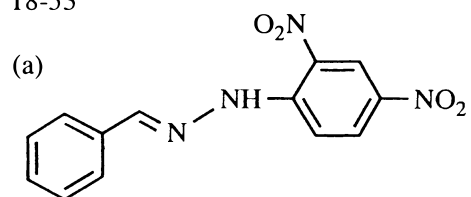
18-51



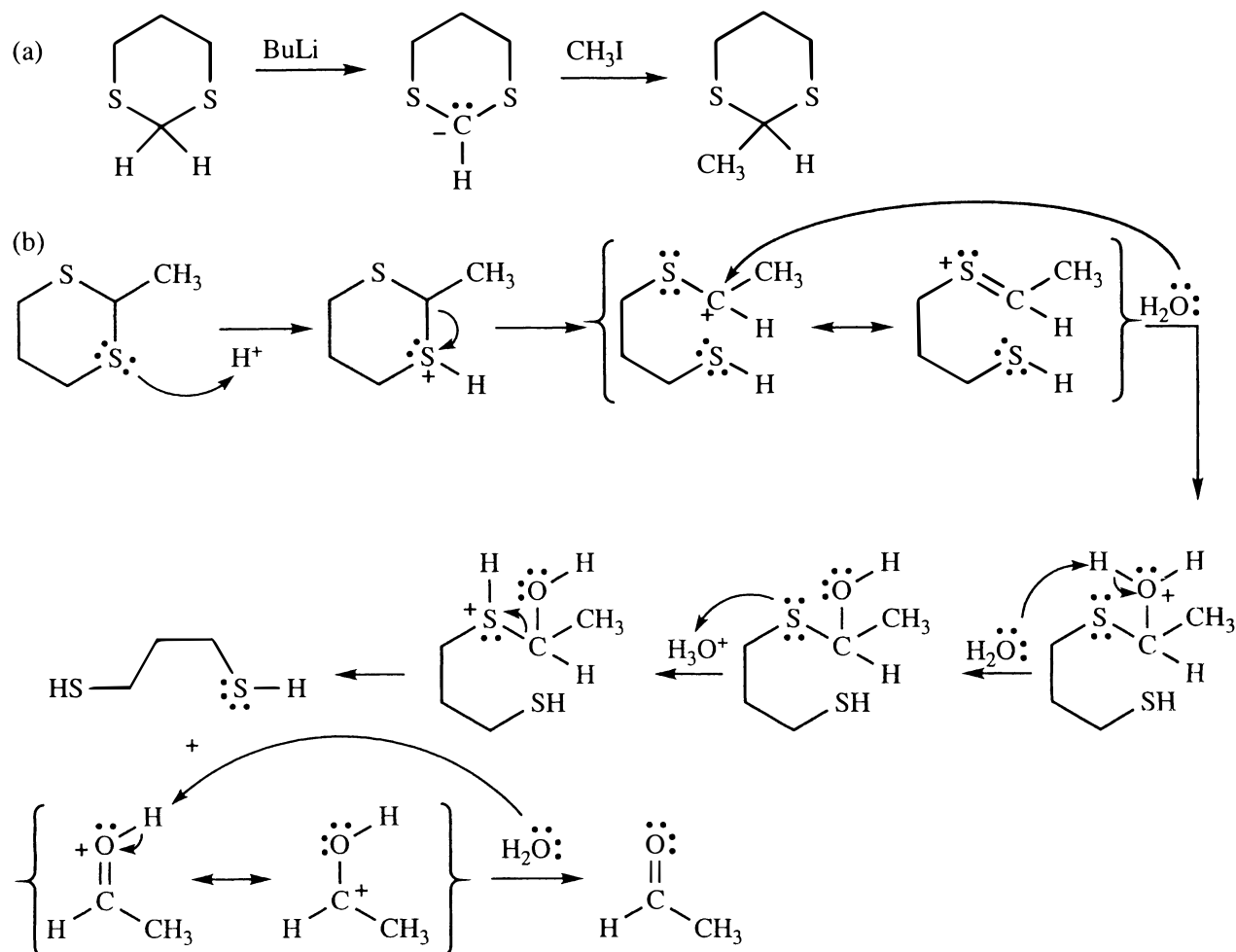
18-52 All of these reactions would be acid-catalyzed.



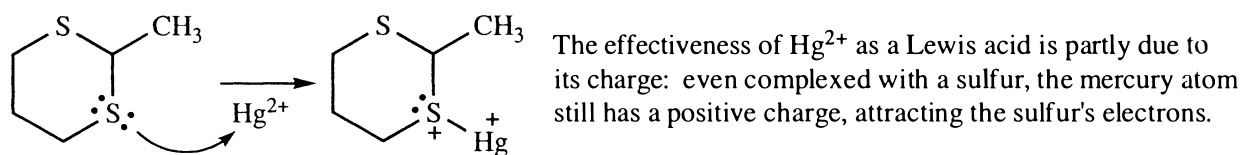
18-53



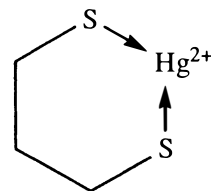
18-54



(c) Mercuric ion, Hg^{2+} , assists the hydrolysis in two ways. First, mercuric ion is a Lewis acid of moderate strength, performing the same function as a proton from a protic acid.

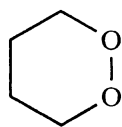


A second explanation for mercuric ion's effectiveness in hydrolysis of thioacetals lies in the complex formed between the ion and the two sulfur atoms. This stable complex effectively removes $\text{HSCH}_2\text{CH}_2\text{SH}$ from the equilibrium, shifting the equilibrium to product. (An example of whose principle? His initials are "Le Châtelier".)



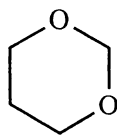
Thiols are often referred to as "mercaptans" because of their ability to CAPTURE MERCURY.

18-55 The key to this problem is understanding that the relative proximity of the two oxygens can dramatically affect their chemistry.



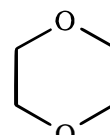
1,2-dioxane

The "second" isomer described: two oxygens connected by a sigma bond are a peroxide. The O—O bond is easily cleaved to give radicals. In the presence of organic compounds, radical reactions can be explosive.



1,3-dioxane

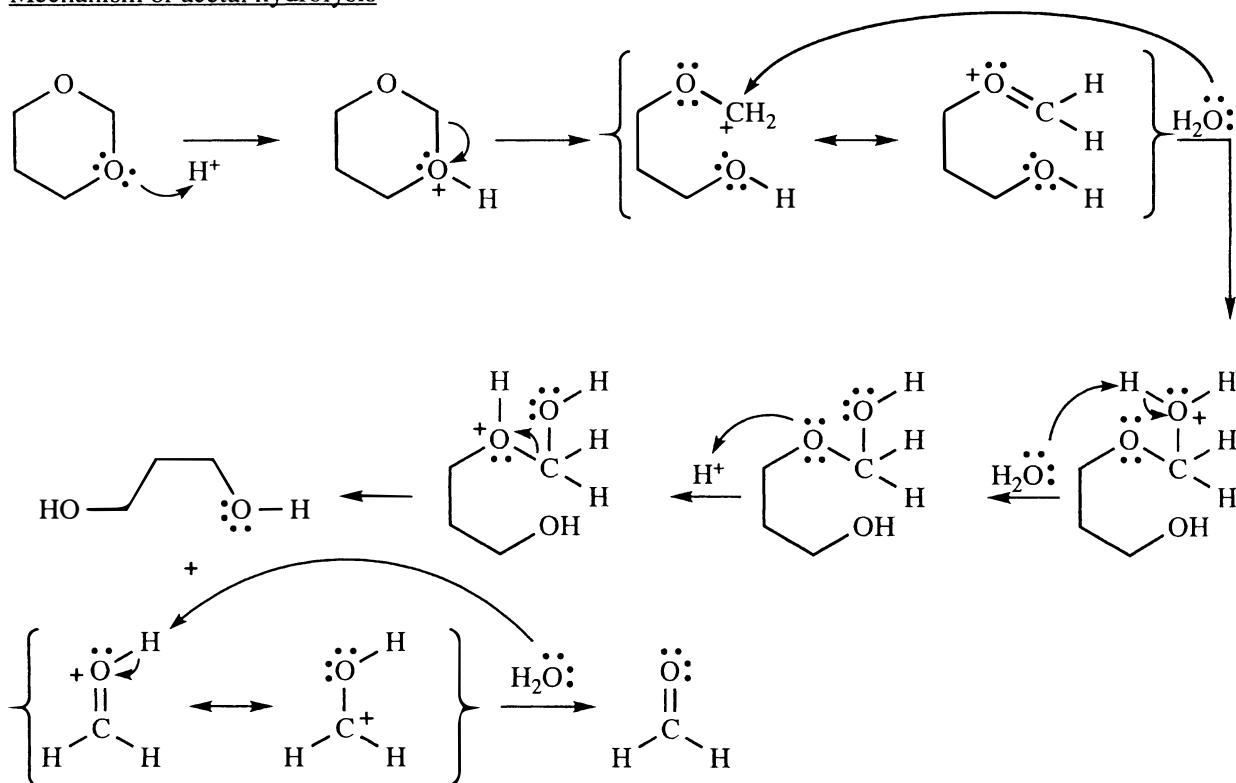
The "third" isomer described: two oxygens bonded to the same sp^3 carbon constitute an acetal which is hydrolyzed in aqueous acid. See the mechanism below.



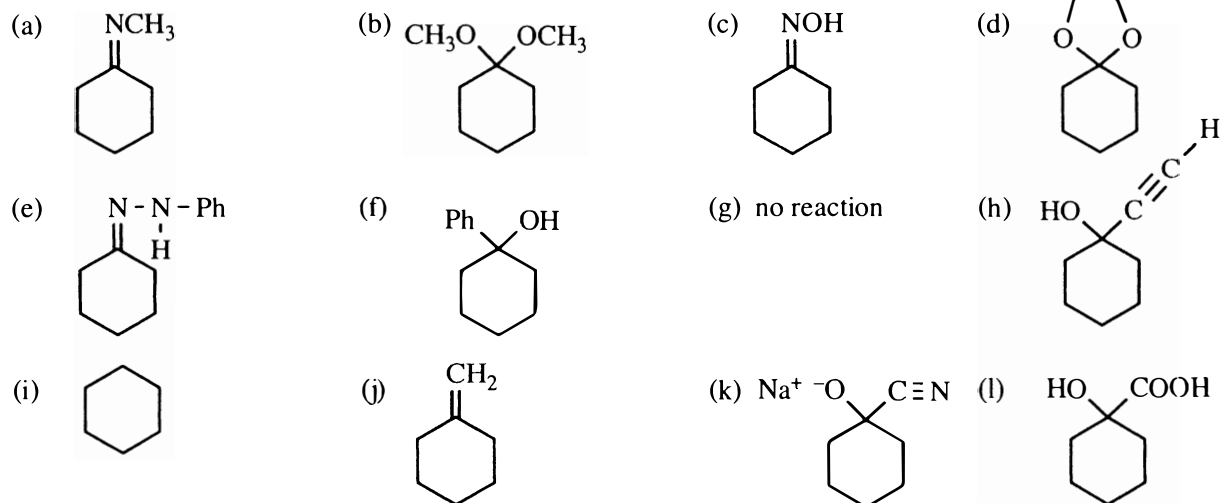
1,4-dioxane

The "first" isomer described: an excellent solvent (although toxic), these oxygens are far enough apart to act independently. It is a simple ether.

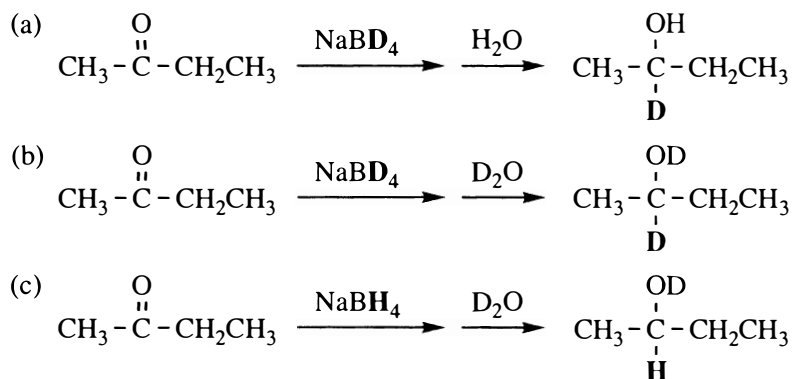
Mechanism of acetal hydrolysis



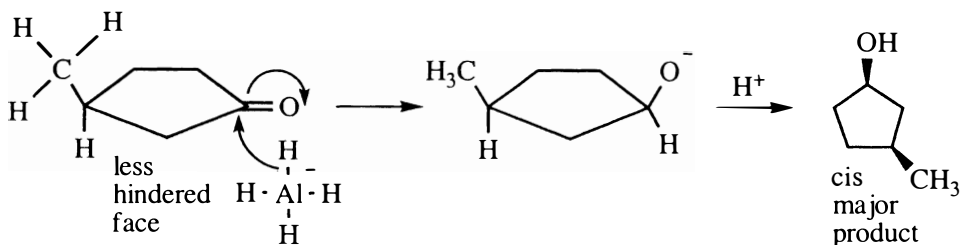
18-56



18-57 The new bond to carbon comes from the NaBH_4 or NaBD_4 , shown in bold below. The new bond to oxygen comes from the protic solvent.

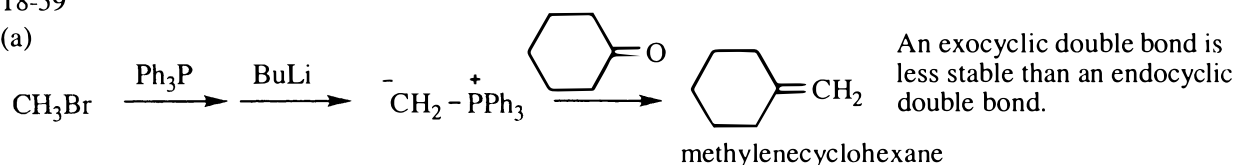


18-58 While hydride is a small group, the actual chemical species supplying it, AlH_4^- , is fairly large, so it prefers to approach from the less hindered side of the molecule, that is, the side opposite the methyl. This forces the oxygen to go to the same side as the methyl, producing the *cis* isomer as the major product.

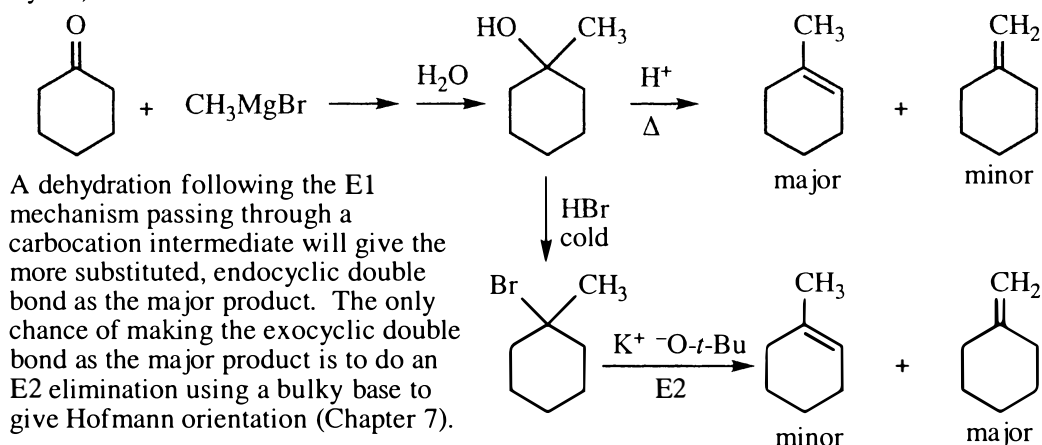


18-59

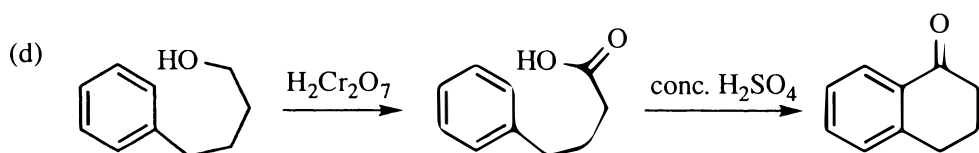
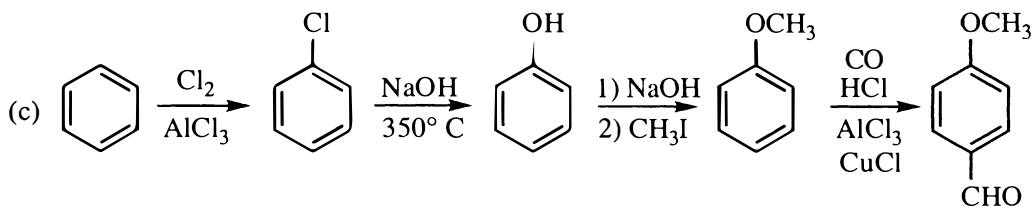
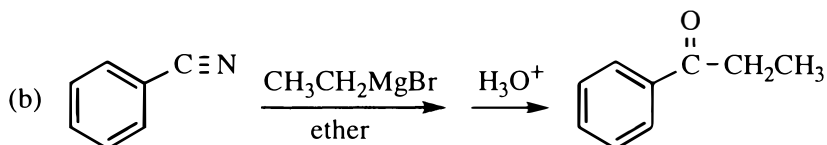
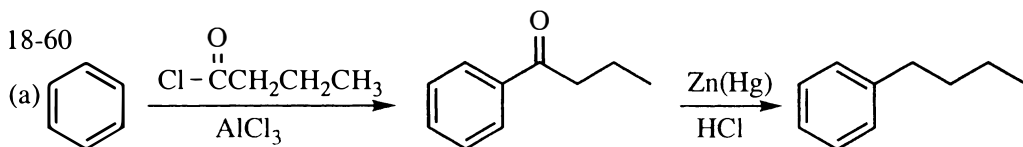
(a)



(b) The difficulty in synthesizing methylenecyclohexane from cyclohexanone without using the Wittig reaction rests in the stability of the double bond inside the ring (endocyclic) versus outside the ring (exocyclic).

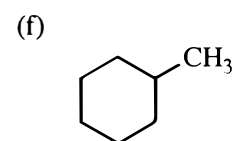
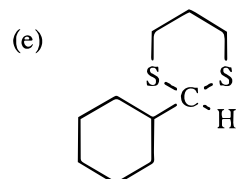
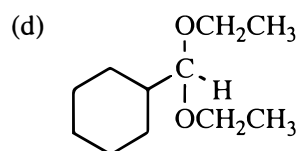
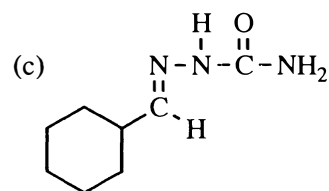
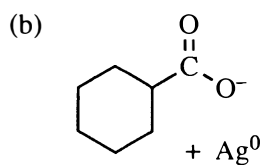
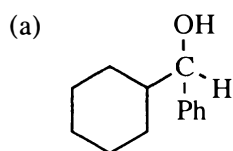


18-60

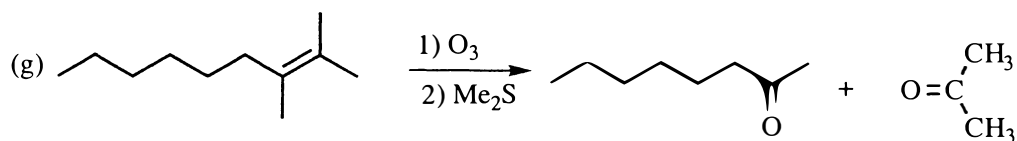
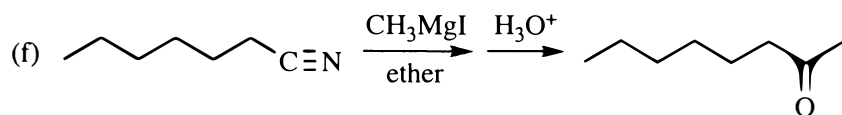
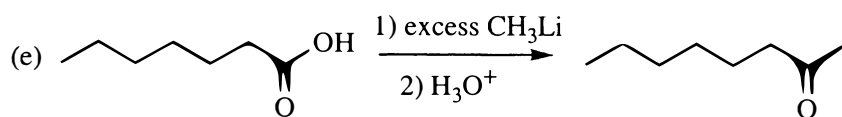
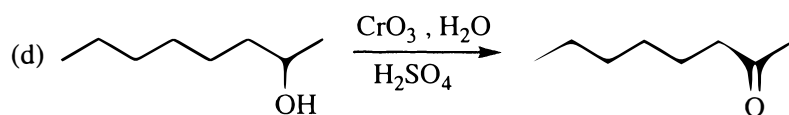
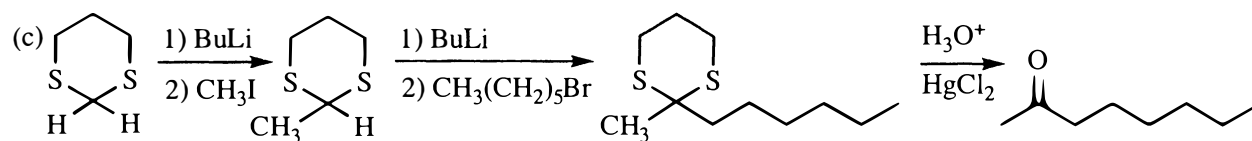
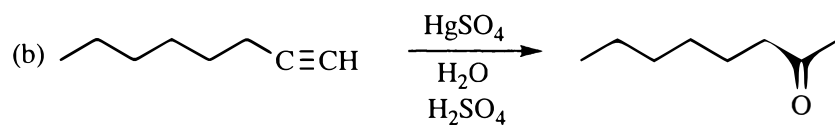
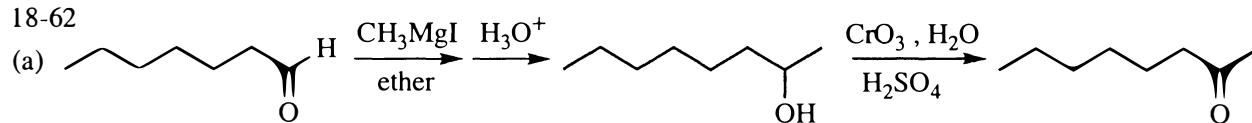


Alternatively, the acid chloride could be made with SOCl_2 , then cyclized by Friedel-Crafts acylation with AlCl_3 .

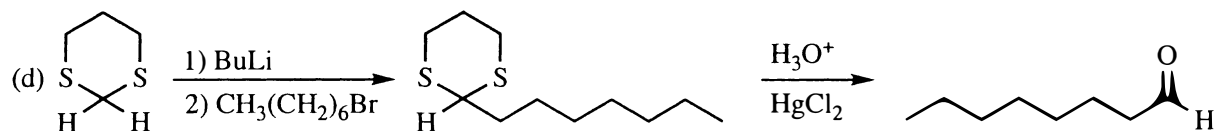
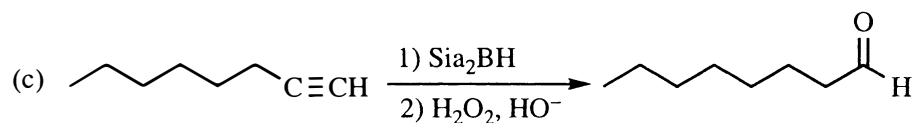
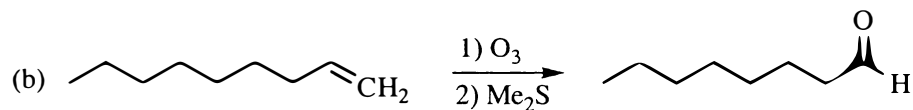
18-61



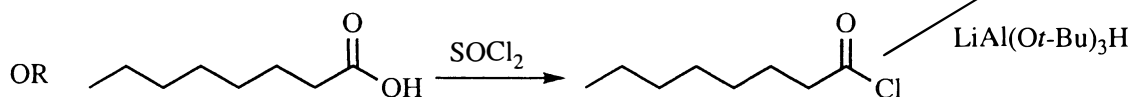
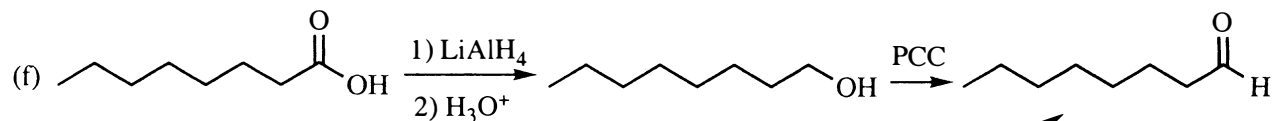
18-62



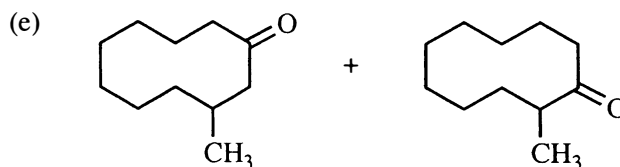
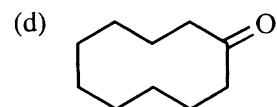
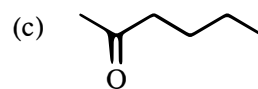
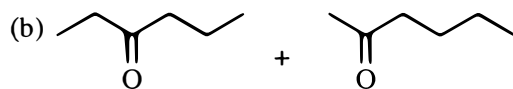
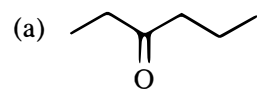
18-63



(This reaction needs a solvent like THF to keep all reactants in solution.)



18-64



18-65

(a) ketone: no reaction

(b) aldehyde: positive

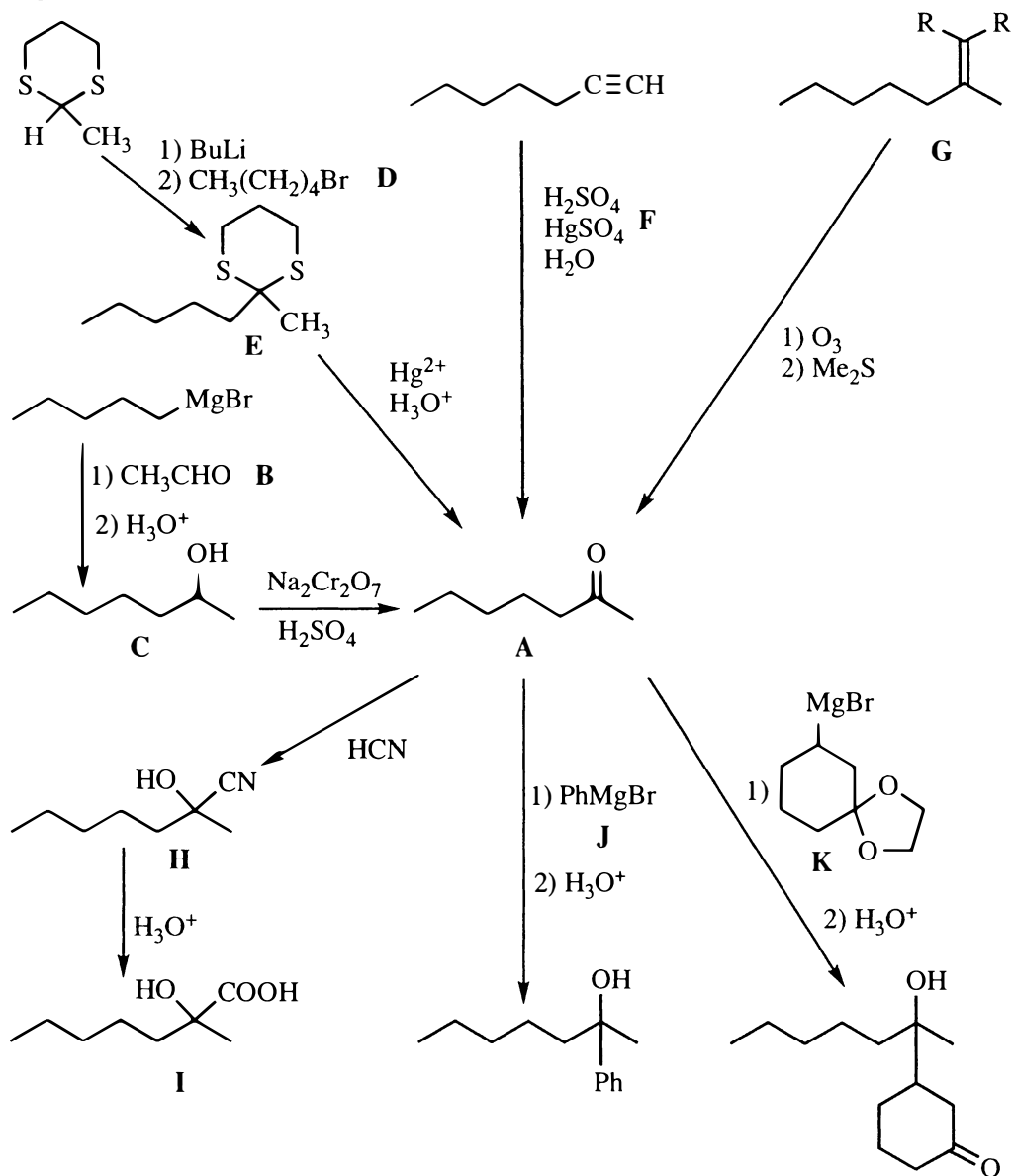
(c) enol of an aldehyde—tautomerizes to aldehyde in base: positive

(d) hemiacetal of an aldehyde in equilibrium with the aldehyde in base: positive

(e) acetal—stable in base: no reaction

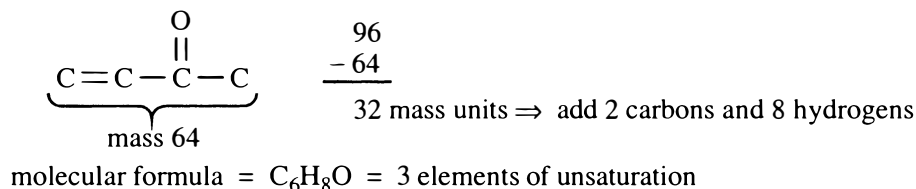
(f) hemiacetal of an aldehyde in equilibrium with the aldehyde in base: positive

18-66 The structure of **A** can be deduced from its reaction with **J** and **K**. What is common to both products of these reactions is the heptan-2-ol part; the reactions must be Grignard reactions with heptan-2-one, so **A** must be heptan-2-one.



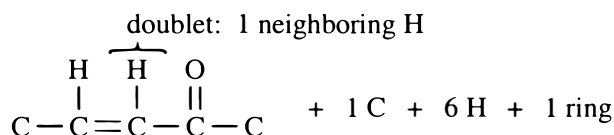
18-67 The very strong π to π^* absorption at 225 nm in the UV spectrum suggests a conjugated ketone or aldehyde. The IR confirms this: strong, conjugated carbonyl at 1690 cm^{-1} and small alkene at 1610 cm^{-1} . The absence of peaks at $2700\text{--}2800\text{ cm}^{-1}$ shows that the unknown is not an aldehyde.

The molecular ion at 96 leads to the molecular formula:

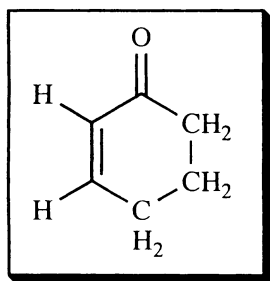


Two elements of unsaturation are accounted for in the enone. The other one is likely a ring.

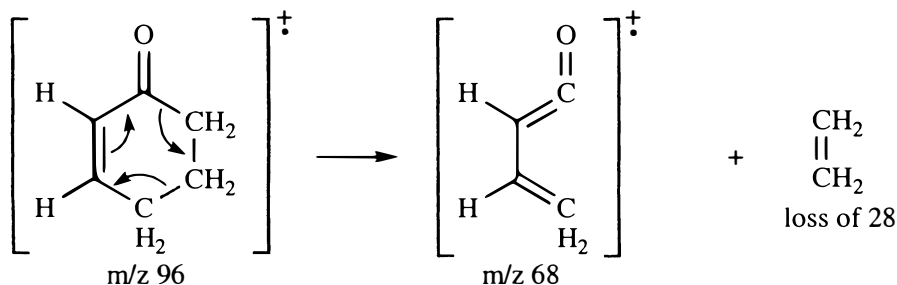
The NMR shows two vinyl hydrogens. The doublet at δ 6.0 says that the two hydrogens are on neighboring carbons (two peaks = one neighboring H).



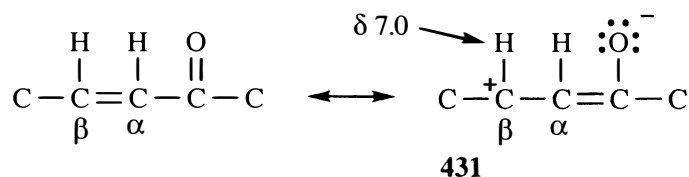
No methyls are apparent in the NMR, so the 6H group of peaks at δ 2.0-2.4 is most likely 3 CH_2 groups. Combining the pieces:



The mass spectral fragmentation can be explained by a "retro" or reverse Diels-Alder fragmentation:

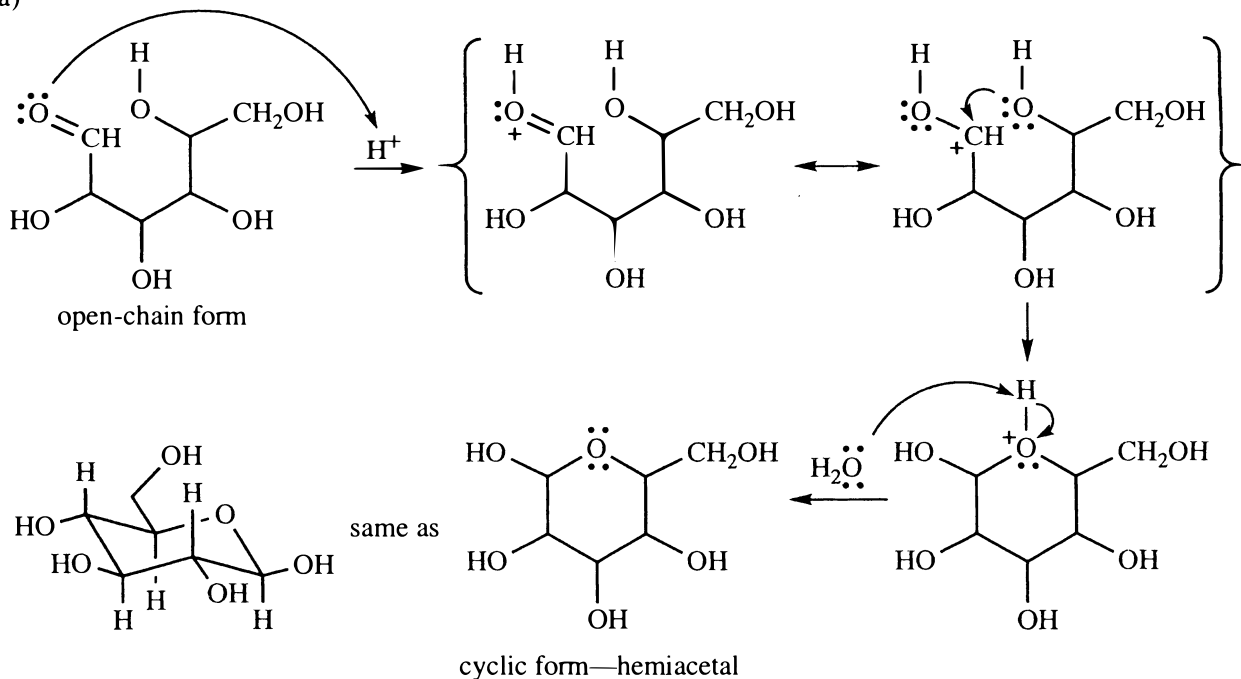


In the HNMR, one of the vinyl hydrogens appears at δ 7.0. This is typical of an α,β -unsaturated carbonyl because of the resonance form that shows deshielding of the β -hydrogen.

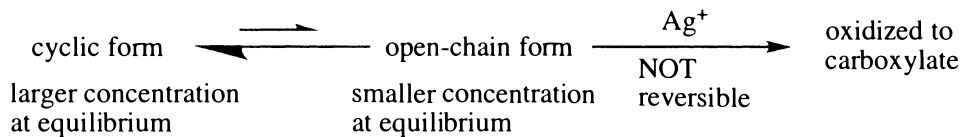


18-68 Building a model will help visualize this problem.

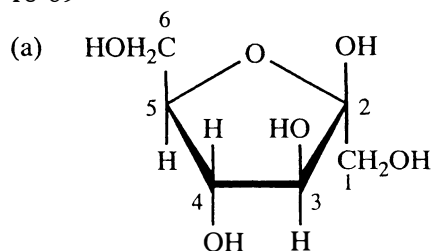
(a)



(b) Yes, the cyclic form of glucose will give a positive Tollens test. In the basic solution of the Tollens test, the hemiacetal is in equilibrium with the open-chain aldehyde with the cyclic form in much larger concentration. However, it is the open-chain aldehyde that reacts with silver ion, so even though there is only a small amount of open-chain form present at any given time, as more of the open-chain form is oxidized by silver ion, more cyclic form will open to replace the consumed open-chain form. Eventually all of the cyclic form will be dragged kicking and screaming through the open-chain form to be oxidized to the carboxylate. Le Châtelier's Principle strikes again!

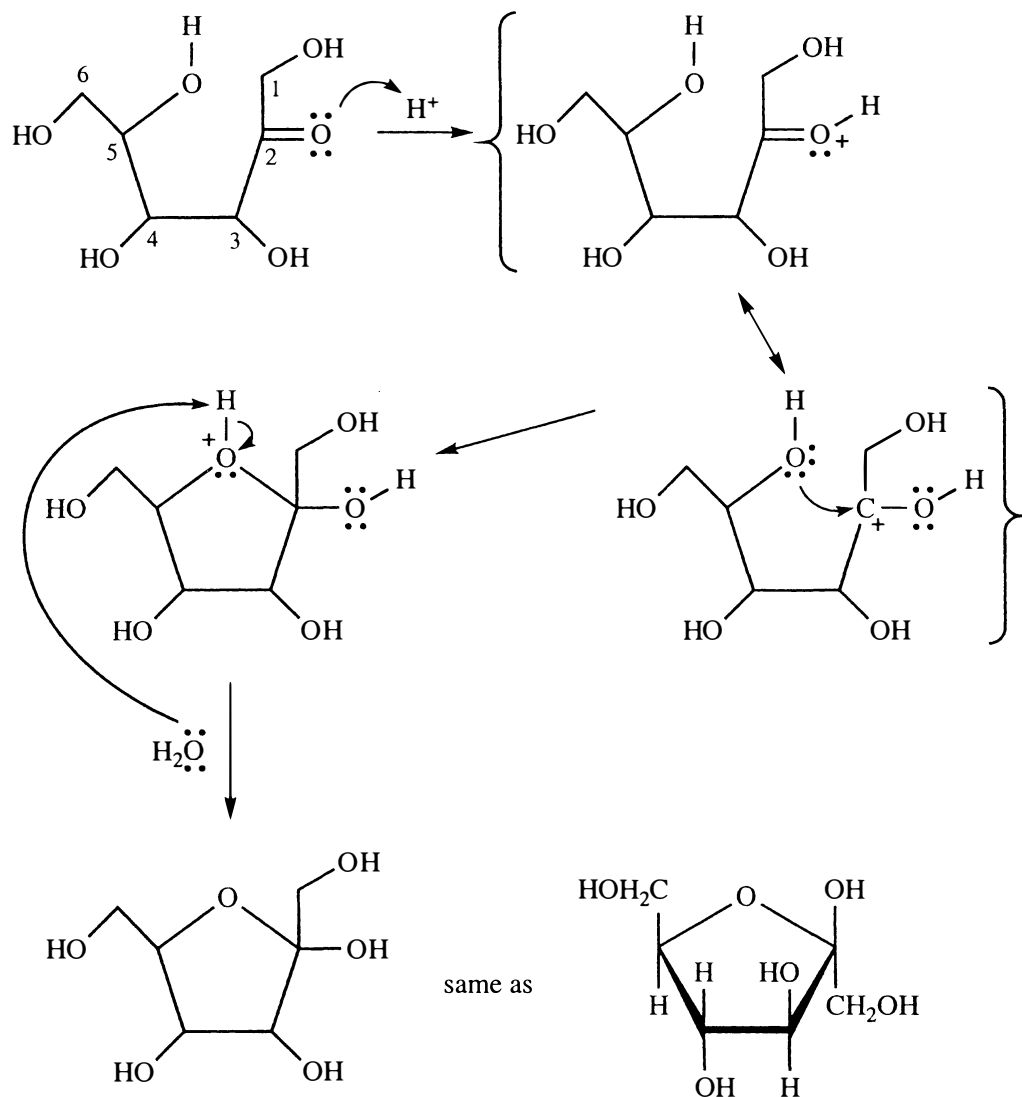


18-69

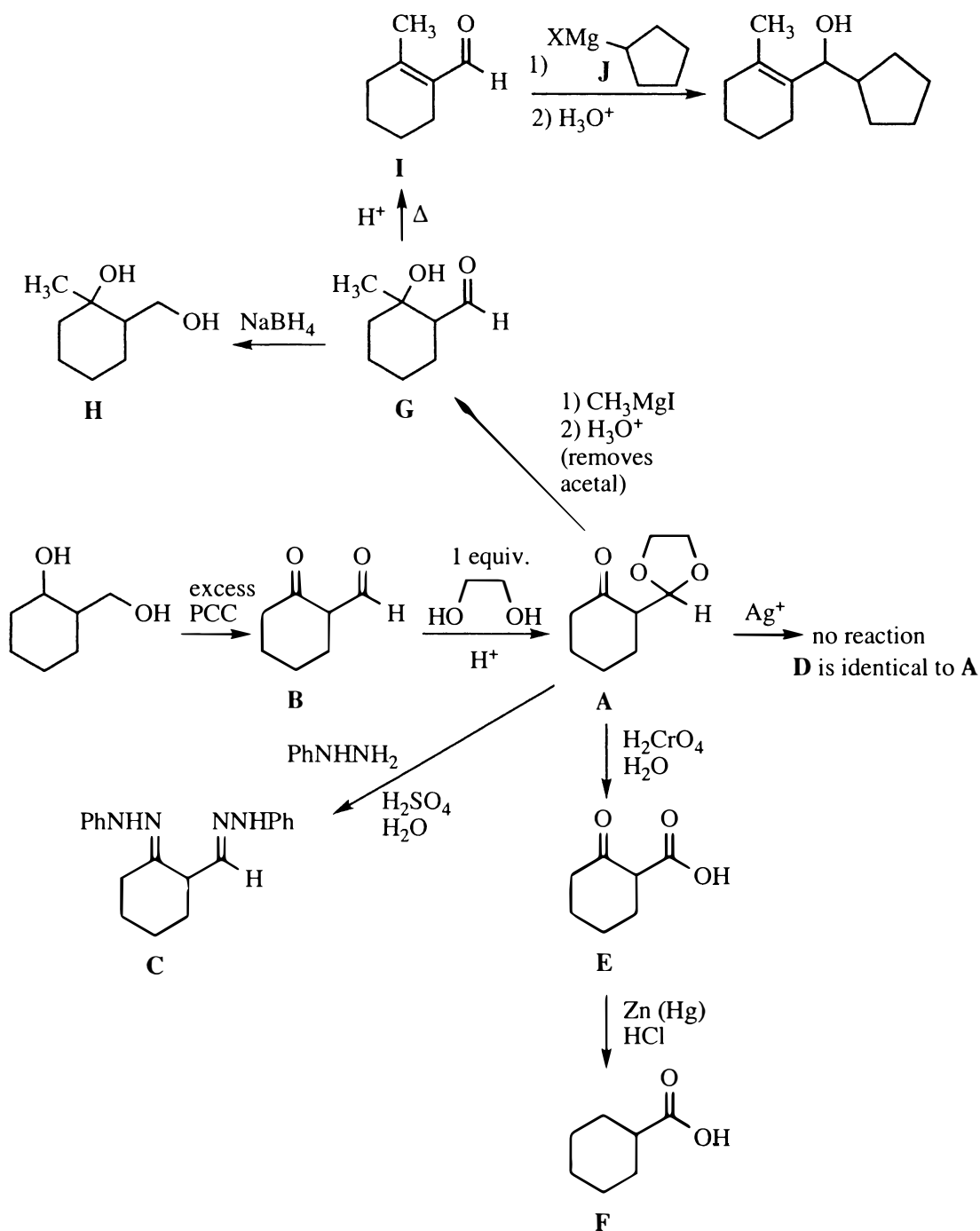


Any carbon with two oxygens bonded to it with single bonds belongs to the acetal family. If one of the oxygen groups is an OH, then the functional group is a hemiacetal. Thus, the functional group at C-2 is a hemiacetal. (The old name for this group is hemiketal as it came from a ketone.)

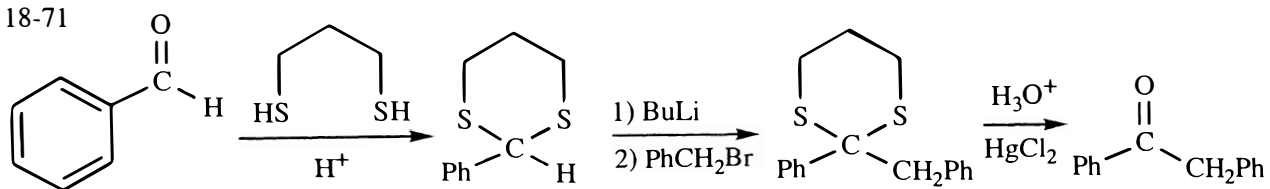
(b) Models will help. Ignore stereochemistry for the mechanism.



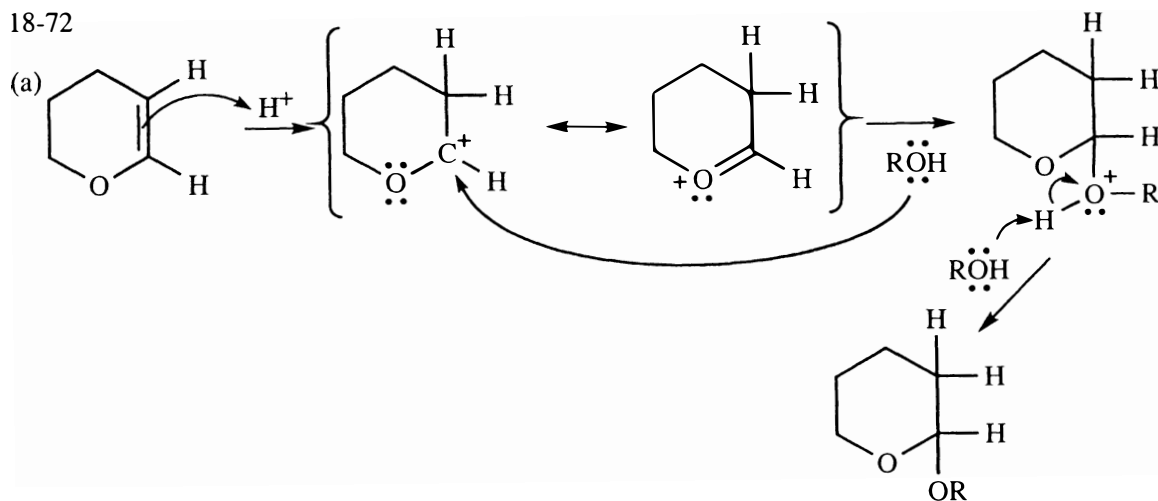
18-70 Recall that "dilute acid" means an aqueous solution, and aqueous acid will remove acetals.



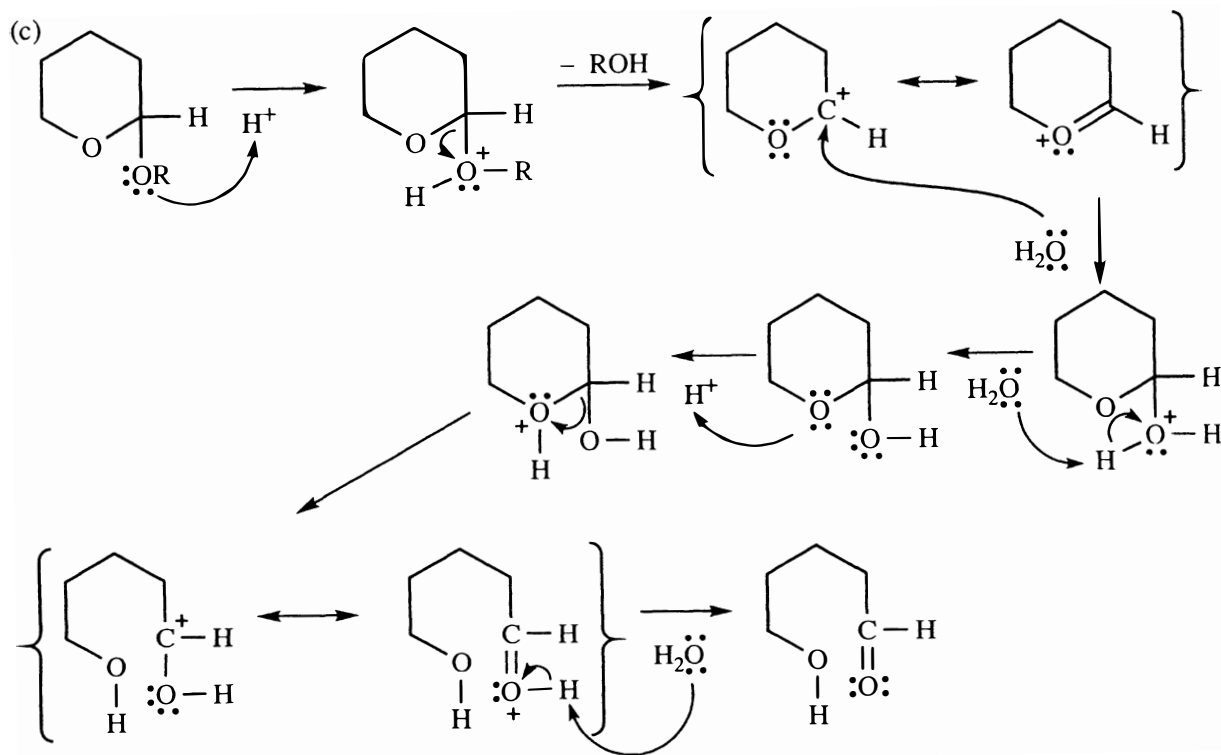
18-71



18-72

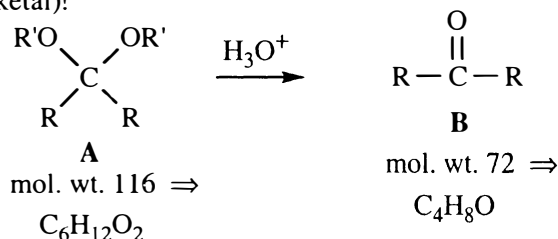


(b) This is not an ether, but rather an acetal, stable to base but reactive with aqueous acid.

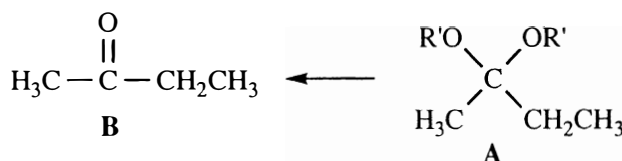


18-73

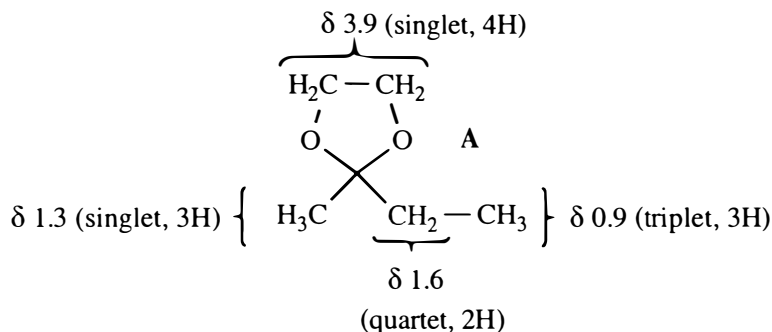
(a) First, deduce what functional groups are present in **A** and **B**. The IR of **A** shows no alkene and no carbonyl: the strongest peak is at 1060 cm^{-1} , possible a C—O bond. After acid hydrolysis of **A**, the IR of **B** shows a carbonyl at 1715 cm^{-1} : a ketone. (If it were an aldehyde, it would have aldehyde C—H around $2700\text{--}2800\text{ cm}^{-1}$, absent in the spectrum of **B**.) What functional group has C—O bonds and is hydrolyzed to a ketone? An acetal (ketal)!



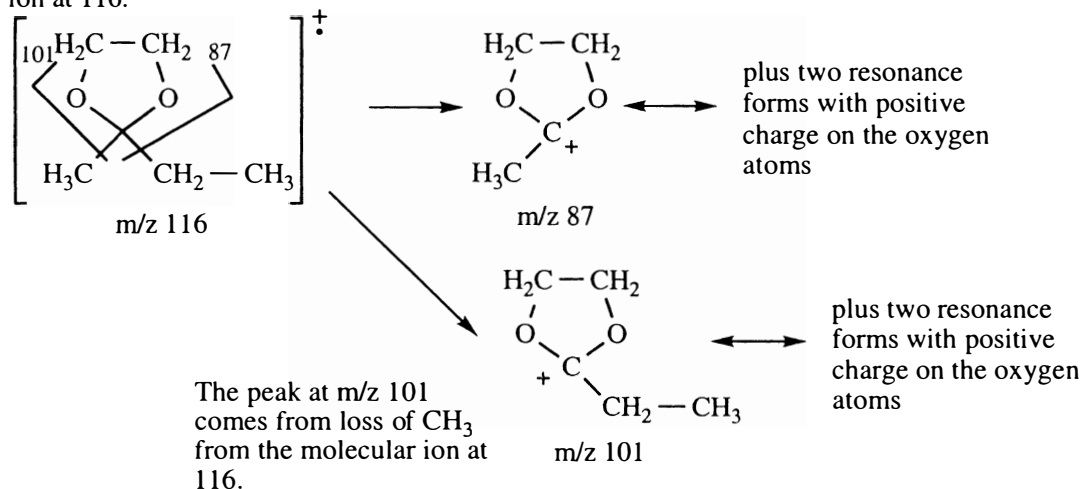
There is only one ketone of formula $\text{C}_4\text{H}_8\text{O}$: butan-2-one.



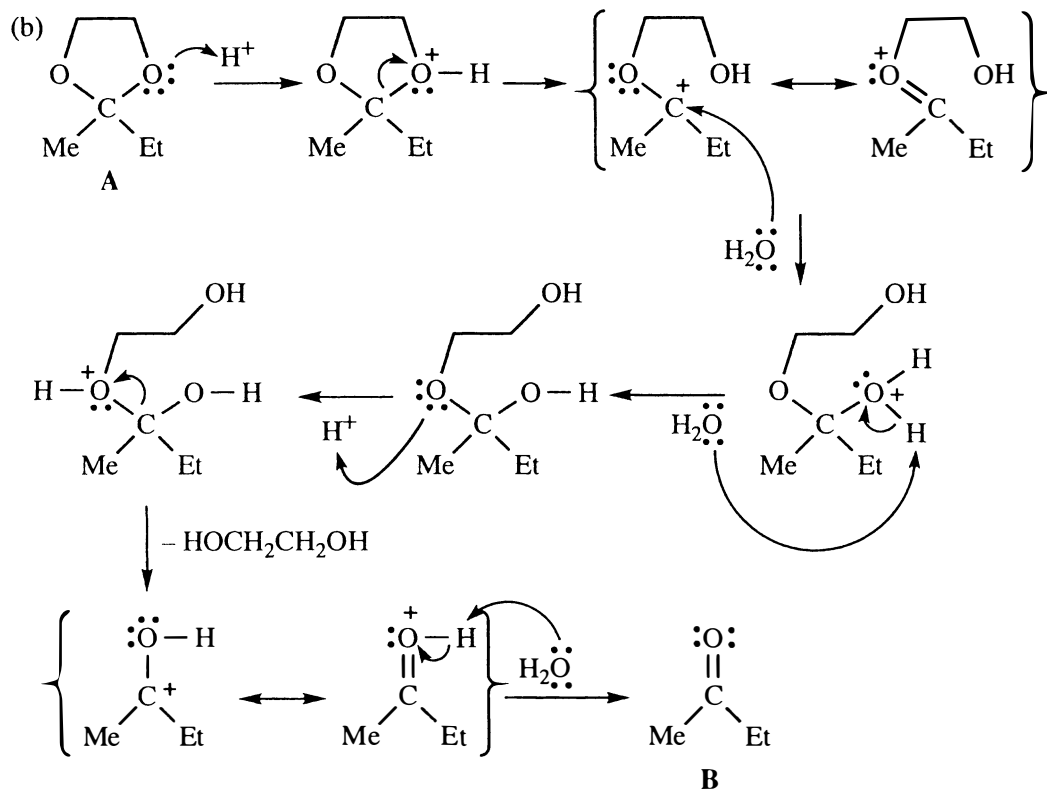
A must have the same alkyl groups as **B**. **A** has one element of unsaturation and is missing only C_2H_4 from the partial structure above. The most likely structure is the ethylene ketal. Is this consistent with the NMR?



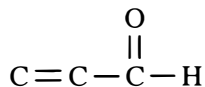
What about the peaks in the MS at m/z 87 and 101? The 87 peak is the loss of 29 from the molecular ion at 116.



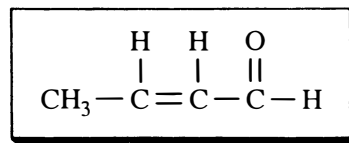
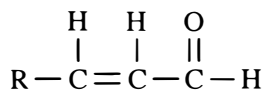
18-73 continued



18-74 The strong UV absorption at 220 nm indicates a conjugated aldehyde or ketone. The IR shows a strong carbonyl at 1690 cm^{-1} , alkene at 1625 cm^{-1} , and two peaks at 2720 cm^{-1} and 2810 cm^{-1} —aldehyde!



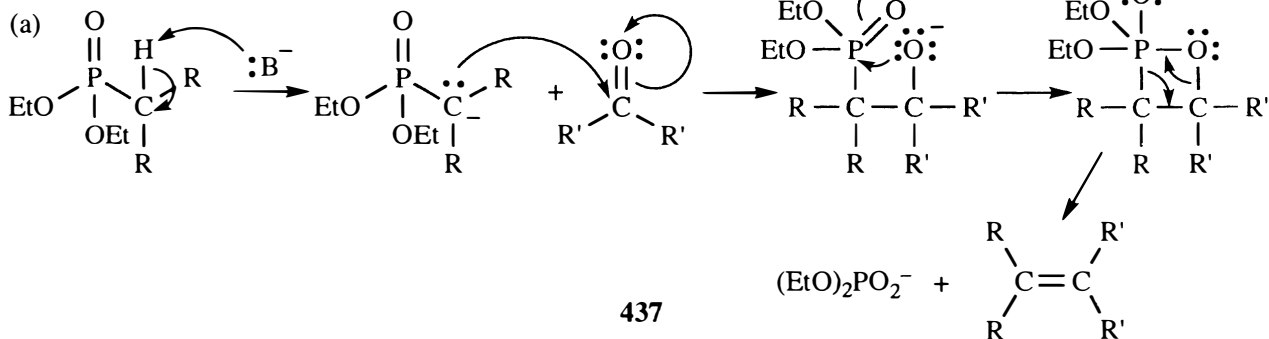
The NMR shows the aldehyde proton at $\delta 9.5$ split into a doublet, so it has one neighboring H. There are only two vinyl protons, so there must be an alkyl group coming off the β carbon:



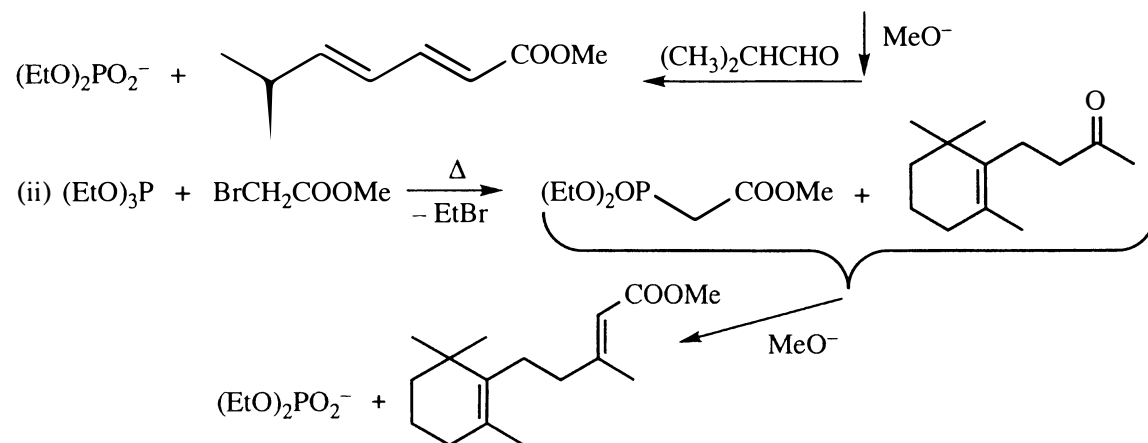
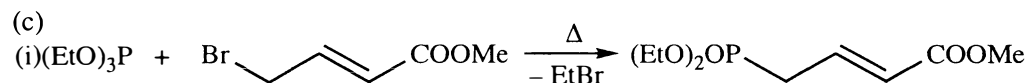
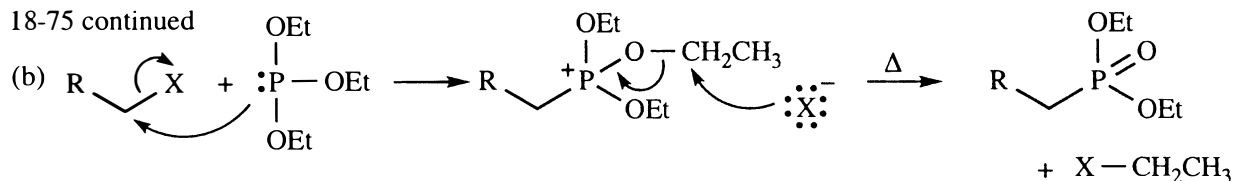
The only other NMR signal is a 3H doublet: R must be methyl.

"crotonaldehyde"

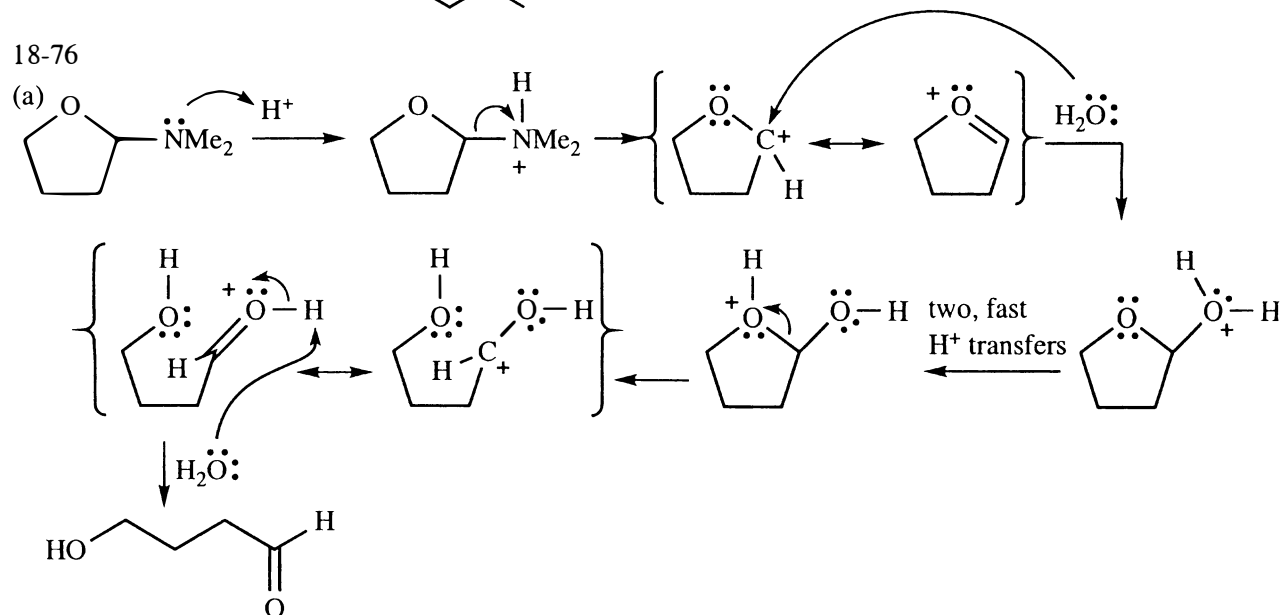
18-75



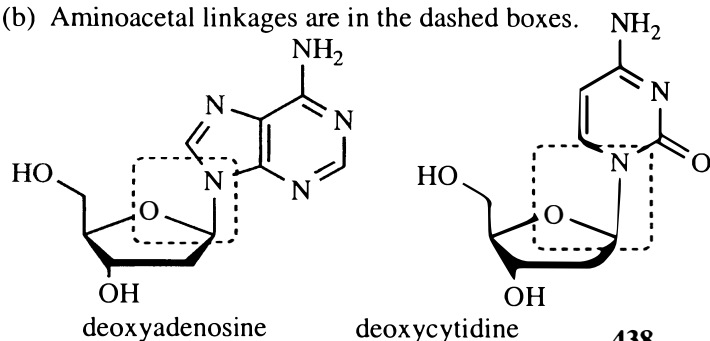
18-75 continued



18-76



(b) Aminoacetal linkages are in the dashed boxes.

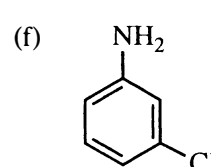
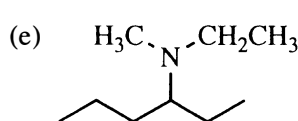
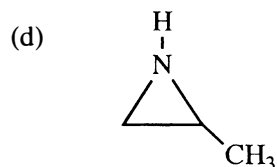
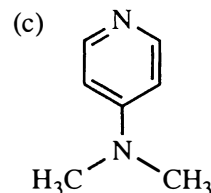
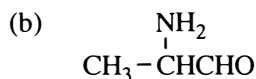
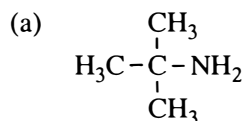


(c) The first step in the mechanism in part (a) is protonation of the amine's electron pair. The nitrogens of the DNA nucleosides, however, are part of aromatic rings, and the electron pairs are required for the aromaticity of the ring. (See the solution to problem 16-42 for a description of the aromaticity of these nucleoside bases.) Protonation of the nitrogen will not occur unless the acid is extremely strong; dilute acids will not protonate the N and therefore the nucleoside will be stable.

CHAPTER 19—AMINES

19-1 These compounds satisfy the criteria for aromaticity (planar, cyclic π system, and the Huckel number of $4n + 2 \pi$ electrons): pyrrole, imidazole, indole, pyridine, 2-methylpyridine, pyrimidine, and purine. The systems with 6 π electrons are: pyrrole, imidazole, pyridine, 2-methylpyridine, and pyrimidine. The systems with 10 π electrons are: indole and purine. The other nitrogen heterocycles shown are not aromatic because they do not have cyclic π systems.

19-2



19-3

- | | |
|--|--|
| (a) pentan-2-amine | (b) <i>N</i> -methylbutan-2-amine |
| (c) 3-aminophenol (or <i>meta</i> -) | (d) 3-methylpyrrole |
| (e) <i>trans</i> -cyclopentane-1,2-diamine | (f) <i>cis</i> -3-aminocyclohexanecarbaldehyde |

19-4

- (a) resolvable: there are two asymmetric carbons; carbon does not invert
(b) not resolvable: the nitrogen is free to invert
(c) not resolvable: it is symmetric
(d) not resolvable: even though the nitrogen is quaternary, one of the groups is a proton which can exchange rapidly, allowing for inversion
(e) resolvable: the nitrogen is quaternary and cannot invert when bonded to carbons

19-5 In order of increasing boiling point (increasing intermolecular hydrogen bonding):

- (a) triethylamine and *n*-propyl ether have the same b.p. < di-*n*-propylamine
(b) dimethyl ether < dimethylamine < ethanol
(c) trimethylamine < diethylamine < diisopropylamine

19-6 Listed in order of increasing basicity. (See Appendix 2 for a discussion of acidity and basicity.)

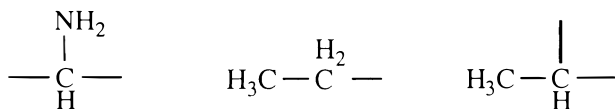
- (a) $\text{PhNH}_2 < \text{NH}_3 < \text{CH}_3\text{NH}_2 < \text{NaOH}$
(b) *p*-nitroaniline < aniline < *p*-methylaniline (*p*-toluidine)
(c) pyrrole < aniline < pyridine
(d) 3-nitropyrrole < pyrrole < imidazole

19-7

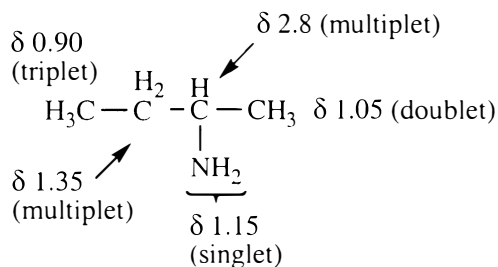
- (a) secondary amine: one peak in the $3200\text{--}3400\text{ cm}^{-1}$ region, indicating NH
(b) primary amine: two peaks in the $3200\text{--}3400\text{ cm}^{-1}$ region, indicating NH_2
(c) alcohol: strong, broad peak around 3400 cm^{-1}

19-8 A compound with formula $C_4H_{11}N$ has no elements of unsaturation. The proton NMR shows five types of H, with the NH_2 appearing as a broad peak at δ 1.15, meaning that there are four different groups of hydrogens on the four carbons. The carbon NMR also shows four carbons, so there is no symmetry in this structure; that is, it does not contain a *t*-butyl group or an isopropyl group.

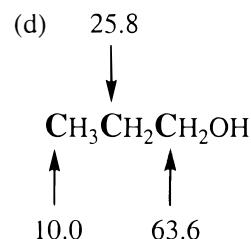
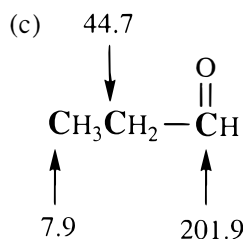
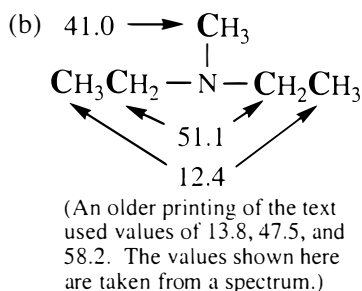
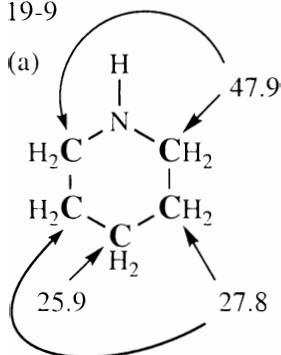
The multiplet farthest downfield is a CH deshielded by the nitrogen; integration shows it to be one H. There is a 2H multiplet at δ 1.35, the broad NH_2 peak at δ 1.15, a 3H doublet at δ 1.05, and a 3H triplet at δ 0.90. The latter two signals must represent methyl groups next to a CH and a CH_2 respectively. So far:



The pieces shown above have one carbon too many, so there must be one carbon that is duplicated: the only possible one is the CH, and the structure reveals itself.

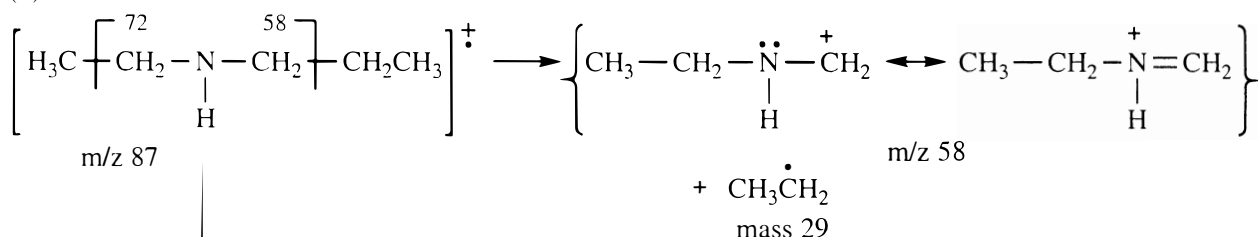


19-9

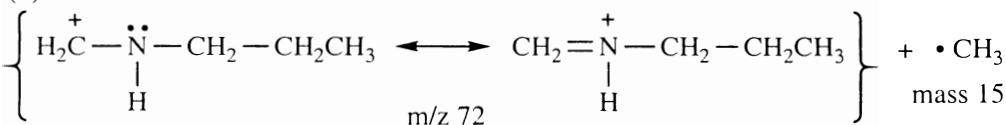


19-10

(a)

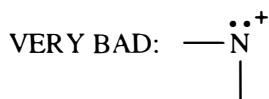
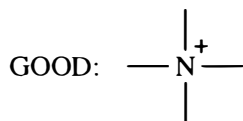


(b)

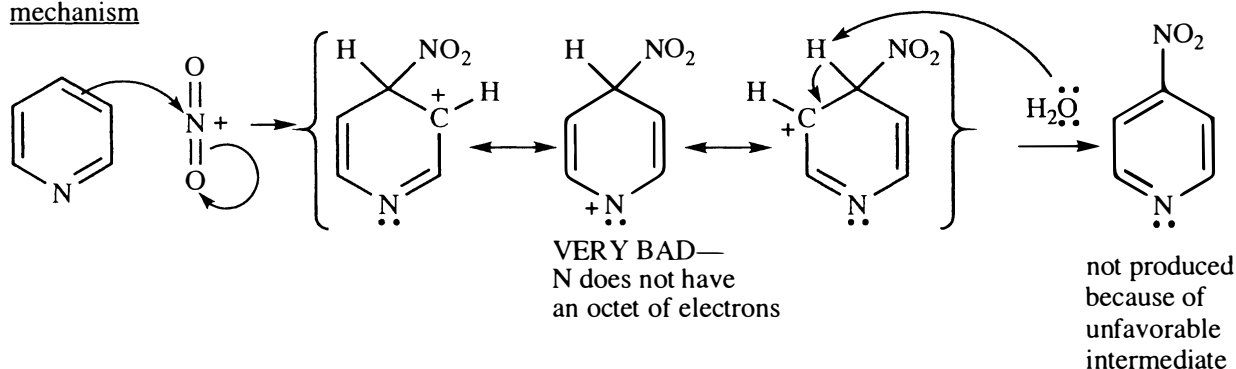


(c) The fragmentation in (a) occurs more often than the one in (b) because of stability of the radicals produced along with the iminium ions. Ethyl radical is much more stable than methyl radical, so pathway (a) is preferred.

19-11 Nitration at the 4-position of pyridine is not observed for the same reason that nitration at the 2-position is not observed: the intermediate puts some positive character on an electron-deficient nitrogen, and electronegative nitrogen hates that. (It is important to distinguish this type of positive nitrogen without a complete octet of electrons, from the quaternary nitrogen, also positively charged but with a full octet. It is the number of electrons around atoms that is most important; the charge itself is less important.)

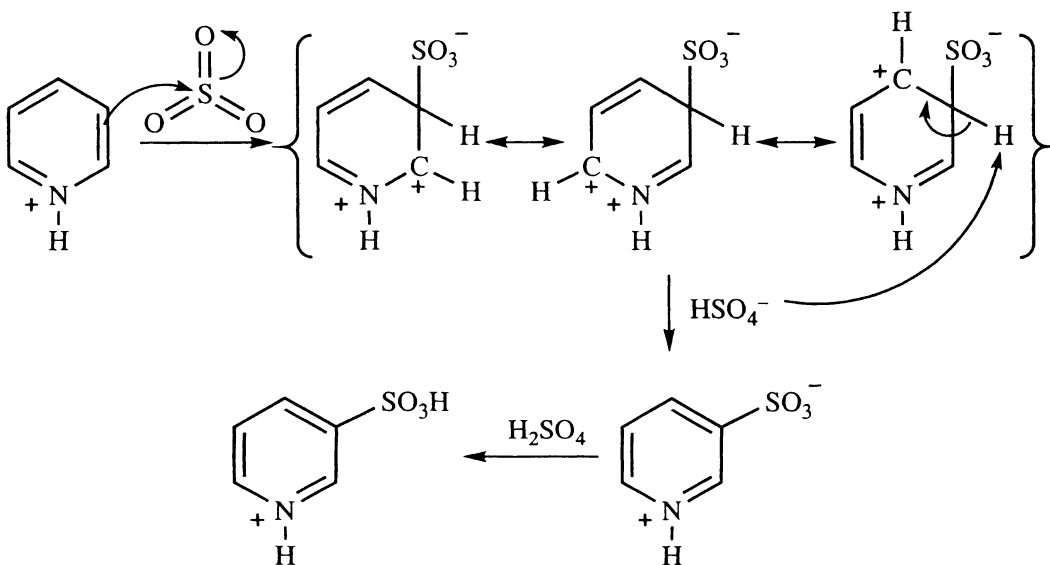


mechanism

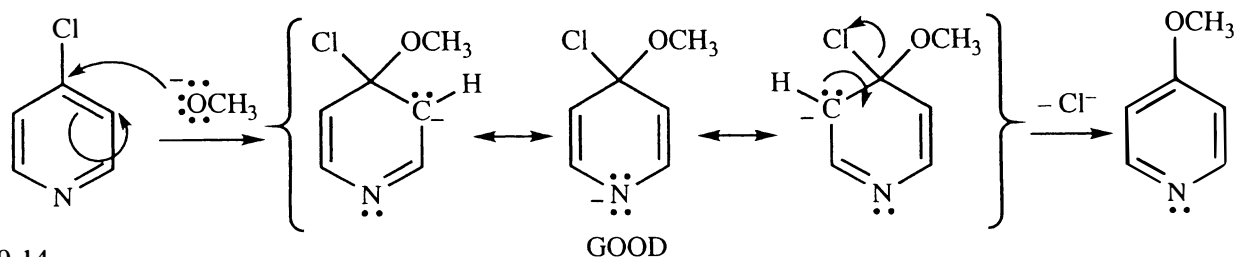


19-12 Any electrophilic attack, including sulfonation, is preferred at the 3-position of pyridine because the intermediate is more stable than the intermediate from attack at either the 2-position or the 4-position. (Resonance forms of the sulfonate group are not shown, but remember that they are important!)

The N of pyridine is basic, and in the strong acid mixture, it will be protonated as shown here. That is part of the reason that pyridine is so sluggish to react: the ring already has a positive charge, so attack of an electrophile is slowed.

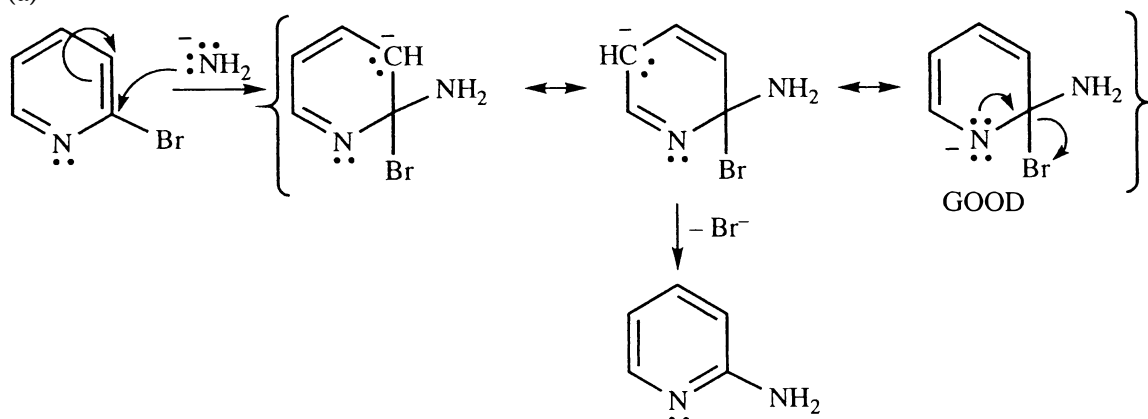


19-13

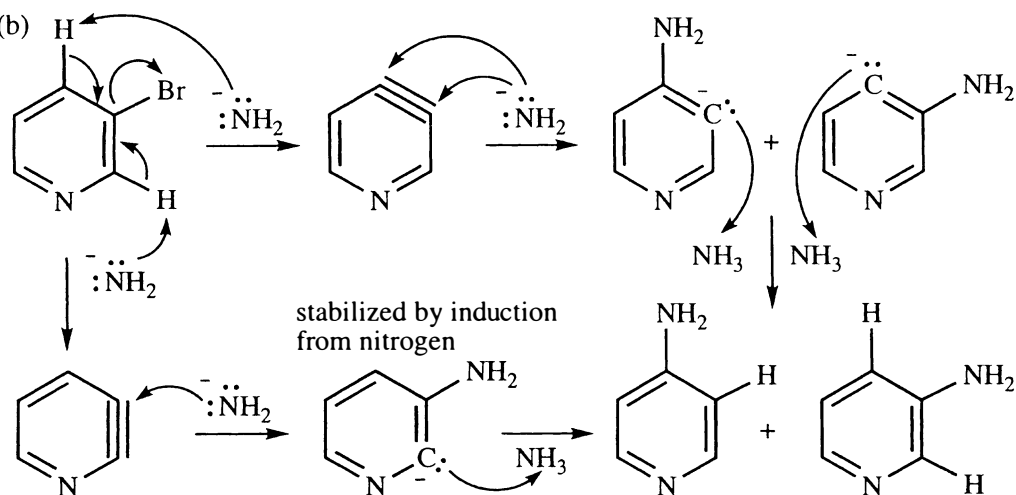


19-14

(a)

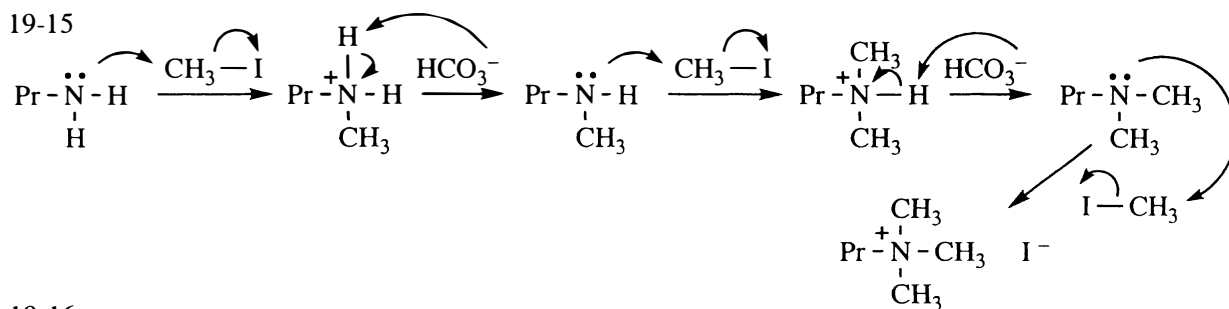


(b)

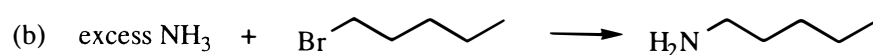
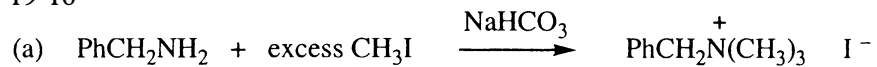


This is a benzyne-type mechanism. (For simplicity above, two steps of benzyne generation are shown as one step: first, a proton is abstracted by amide anion, followed by loss of bromide.) Amide ion is a strong enough base to remove a proton from 3-bromopyridine as it does from a halobenzene. Once a benzyne is generated (two possibilities), the amide ion reacts quickly, forming a mixture of products.

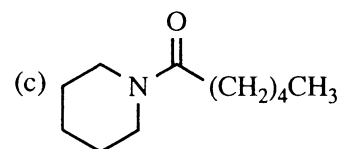
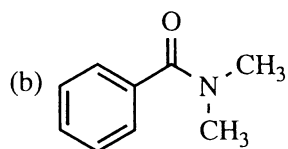
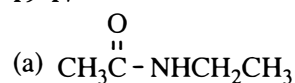
Why does the 3-bromo follow this extreme mechanism while the 2-bromo reacts smoothly by the addition-elimination mechanism? Stability of the intermediate! Negative charge on the electronegative nitrogen makes for a more stable intermediate in the 2-bromo substitution. No such stabilization is possible in the 3-bromo case.



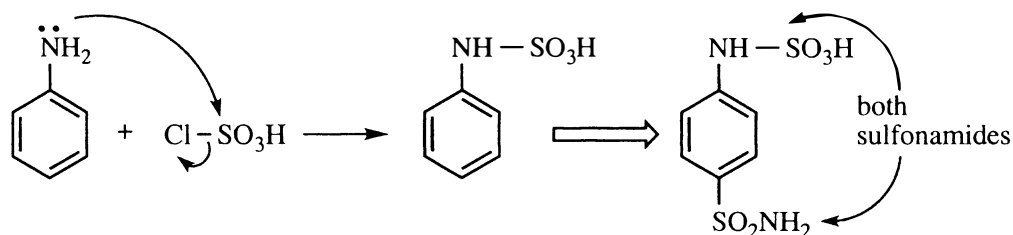
19-16



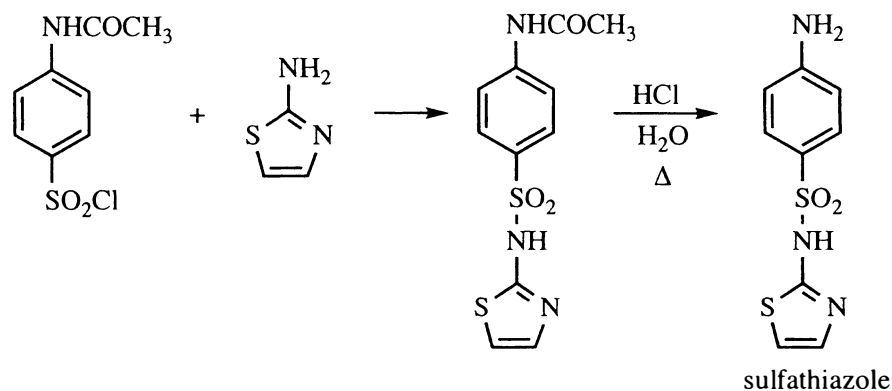
19-17



19-18 If the amino group were not protected, it would do a nucleophilic substitution on chlorosulfonic acid. Later in the sequence, this group could not be removed without cleaving the other sulfonamide group.

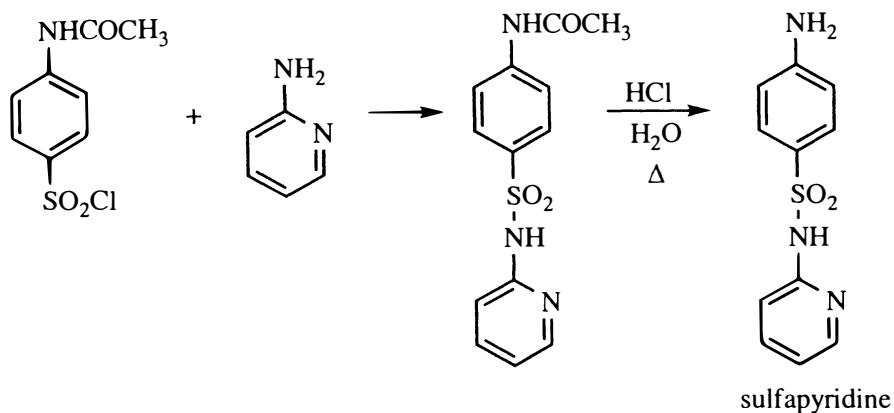


19-19

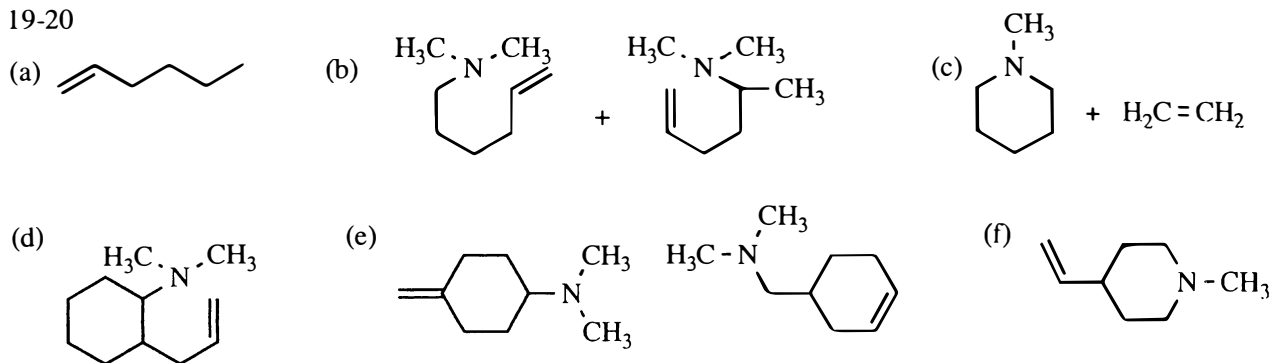


continued on next page

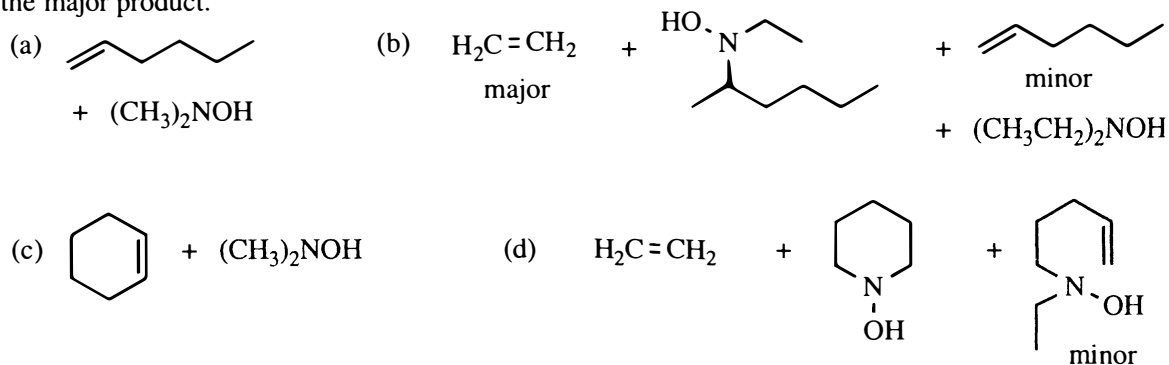
19-19 continued



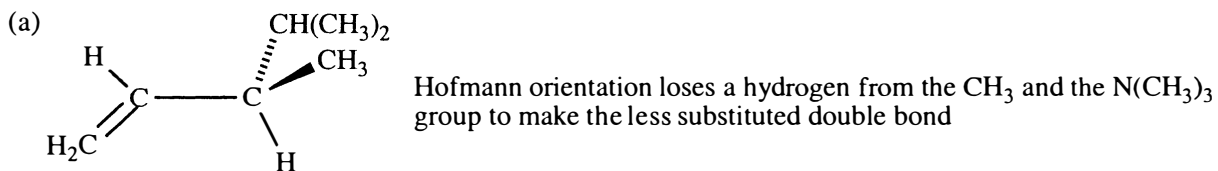
19-20



19-21 Orientation of the Cope elimination is similar to Hofmann elimination: the *less* substituted alkene is the major product.

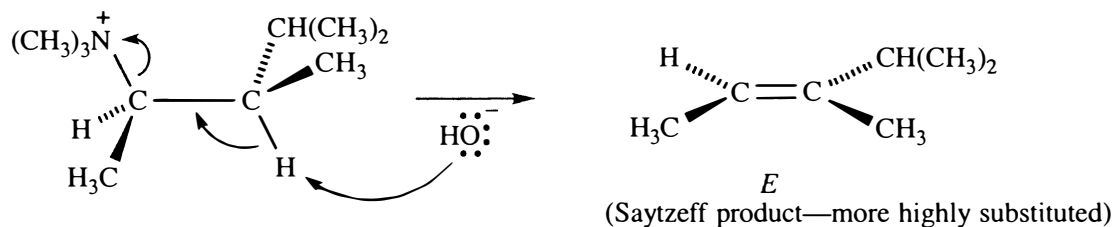


19-22 The key to this problem is to understand that Hofmann elimination occurs via an E2 mechanism requiring *anti* coplanar stereochemistry, whereas Cope elimination requires *syn* coplanar stereochemistry.

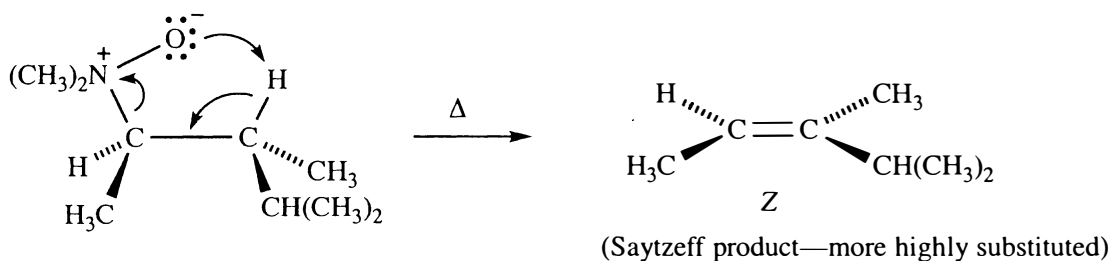


19-22 continued

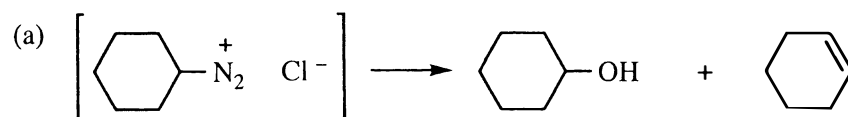
(b) Hofmann elimination



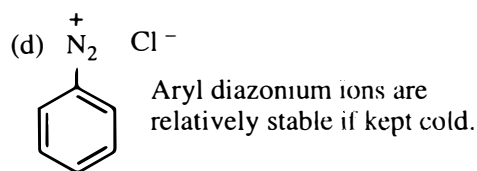
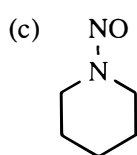
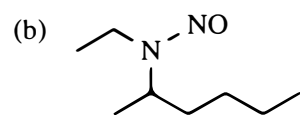
Cope elimination



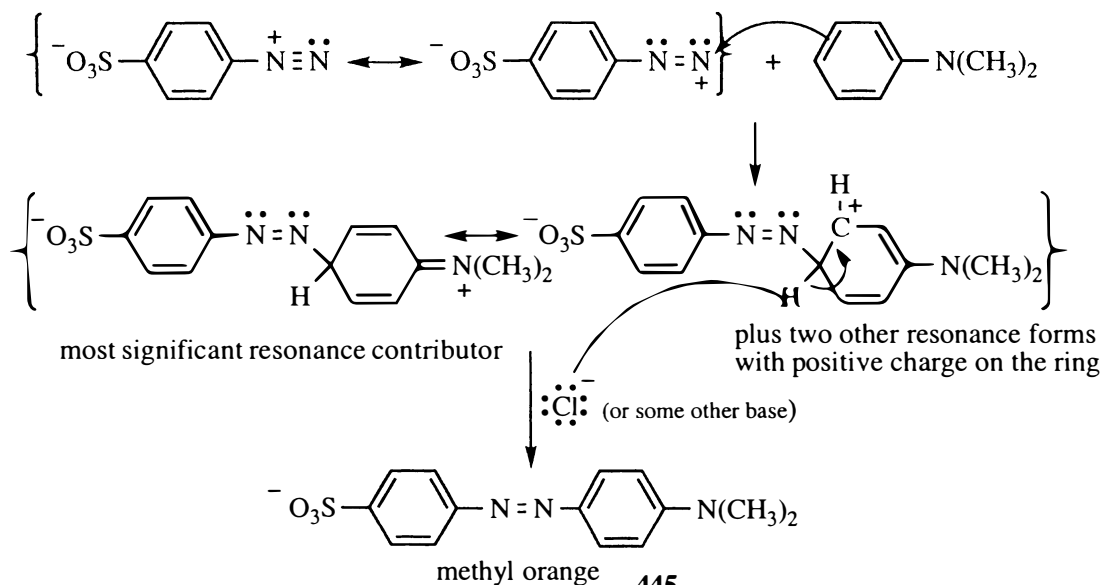
19-23



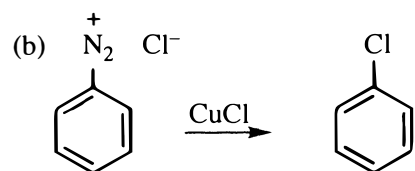
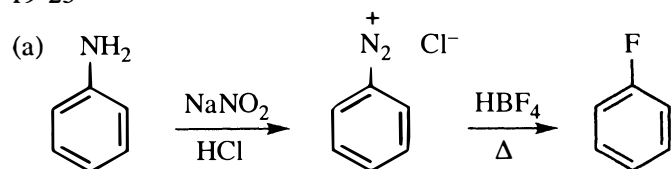
Aliphatic diazonium ions are very unstable, rapidly decomposing to carbocations.



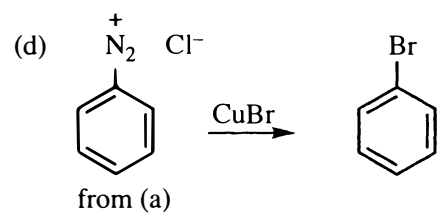
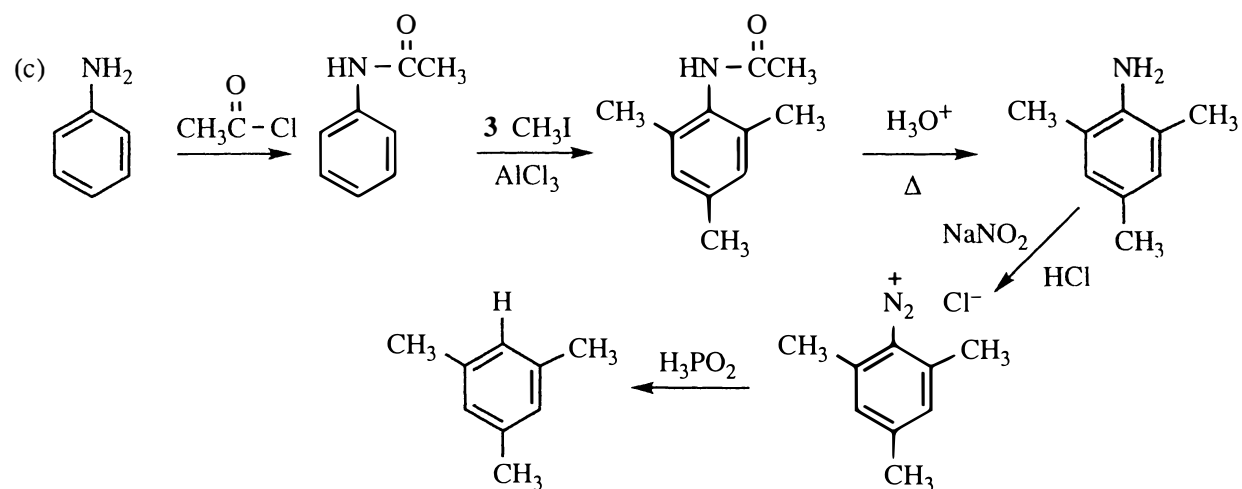
19-24 The diazonium ion can do aromatic substitution like any other electrophile.



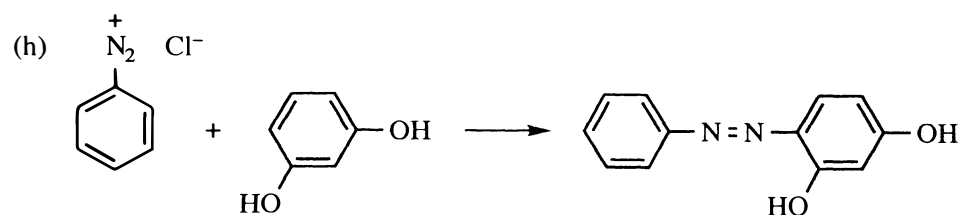
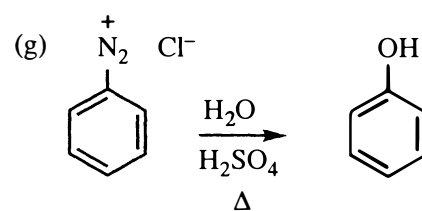
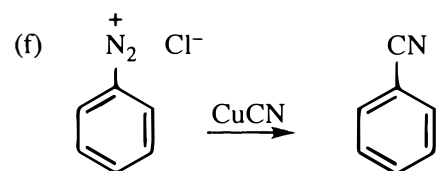
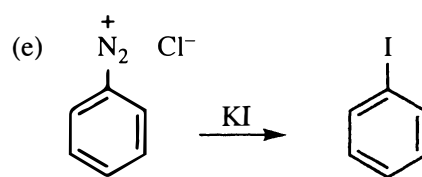
19-25



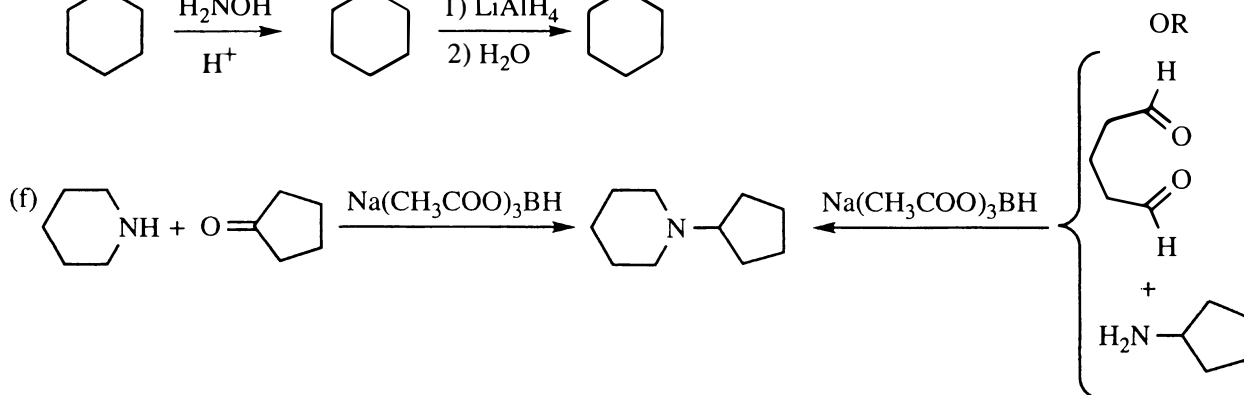
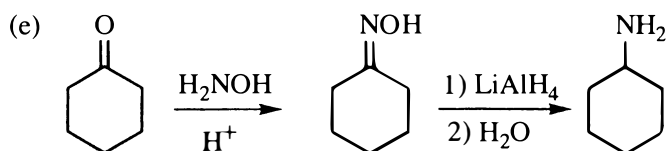
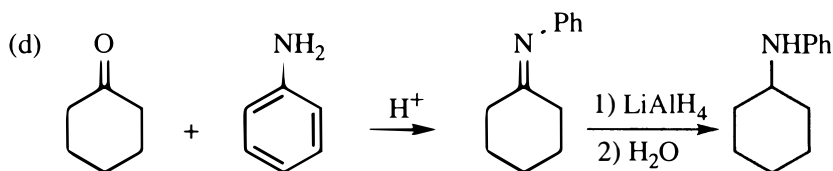
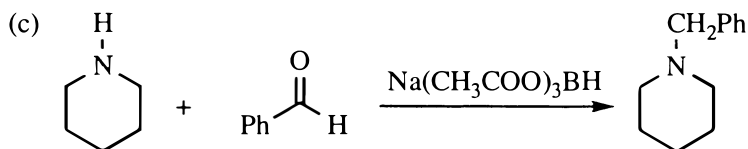
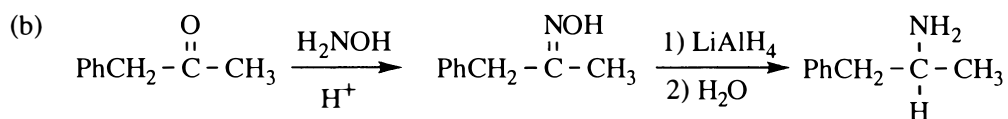
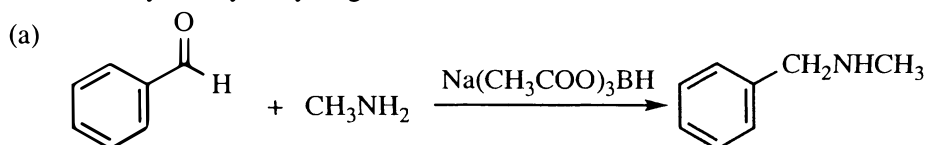
from (a)



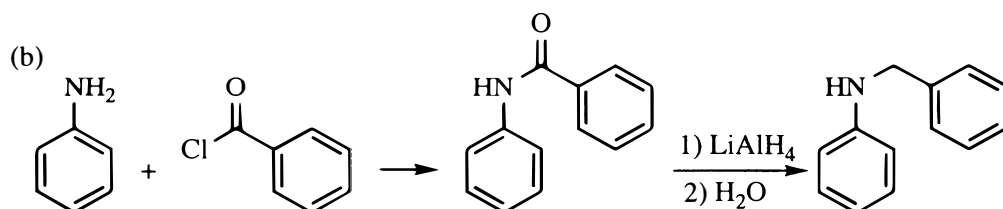
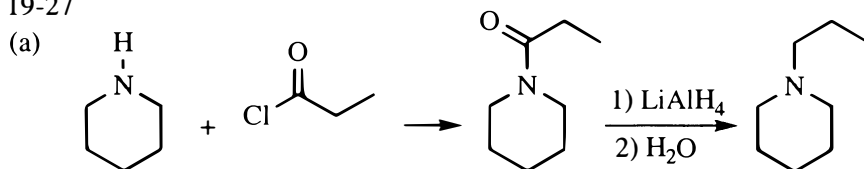
from (a)



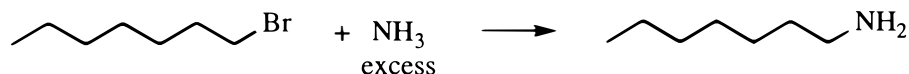
19-26 General guidelines for choice of reagent for reductive amination: use LiAlH_4 when the imine or oxime is isolated. Use $\text{Na}(\text{CH}_3\text{COO})_3\text{BH}$ in solution when the imine or iminium ion is not isolated. Alternatively, catalytic hydrogenation works in most cases.



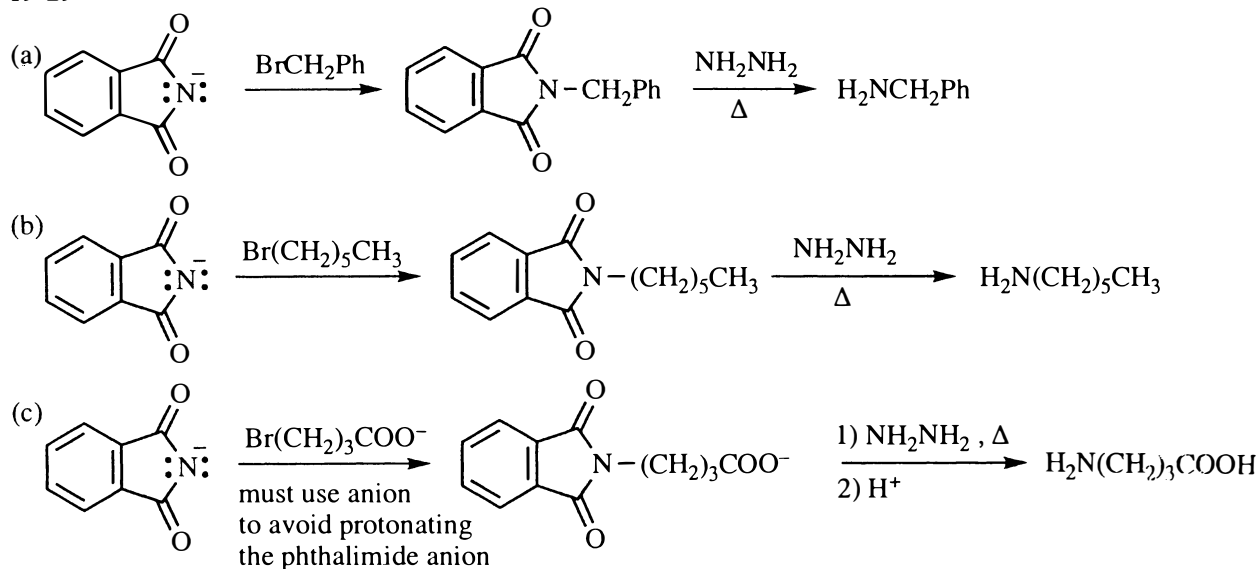
19-27



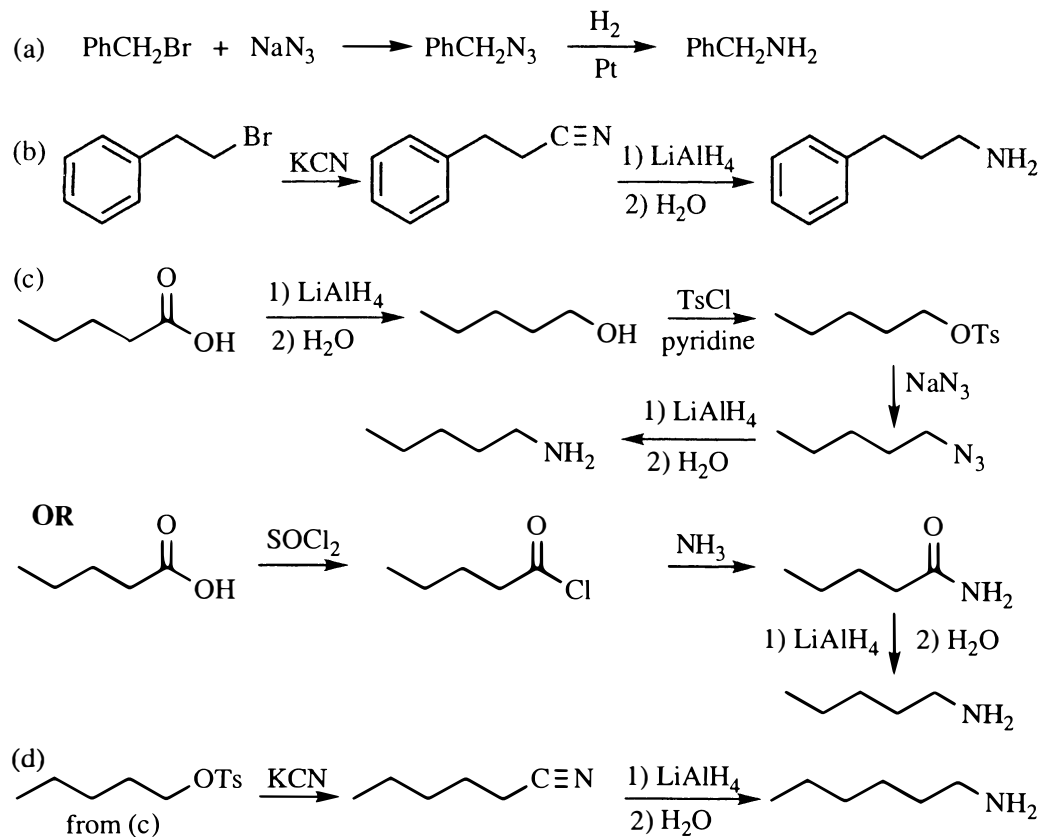
19-28 Use a large excess of ammonia to avoid multiple alkylations of each nitrogen.

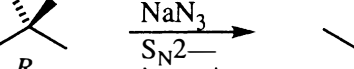


19-29

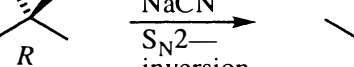


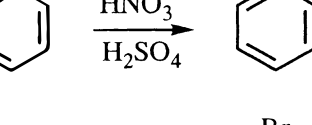
19-30 Assume that LiAlH_4 or $\text{H}_2/\text{catalyst}$ can be used interchangeably.

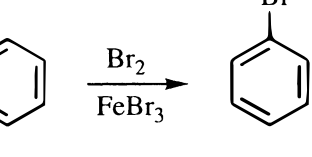


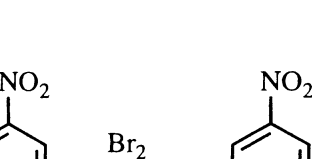
(e) 
 $\text{(R)-2-bromobutane} \xrightarrow[\text{inversion}]{\text{NaN}_3, \text{S}_{\text{N}}2} \text{(S)-2-azidobutane} \xrightarrow[2) \text{H}_2\text{O}]{1) \text{LiAlH}_4} \text{(S)-2-butylamine}$

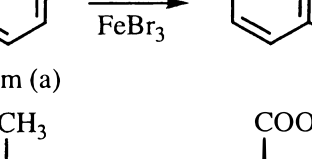
(f) 
 $\text{(R)-2-bromobutane} \xrightarrow[\text{inversion}]{\text{NaCN}, \text{S}_{\text{N}}2} \text{(S)-2-pentanenitrile} \xrightarrow[2) \text{H}_2\text{O}]{1) \text{LiAlH}_4} \text{(S)-2-pentylamine}$

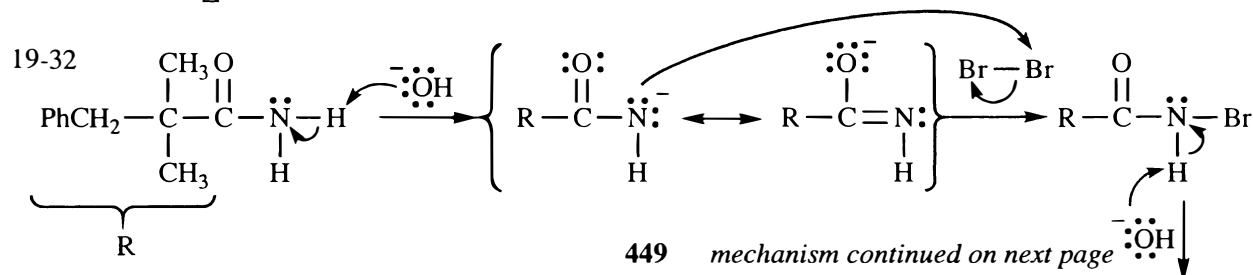
(g) 
 $\text{2-pentanone} \xrightarrow[\text{HCN}]{\text{KCN}} \text{2-hydroxy-2-methylpentanenitrile} \xrightarrow[2) \text{H}_2\text{O}]{1) \text{LiAlH}_4} \text{2-amino-2-methylpentan-2-ol}$

(a) 

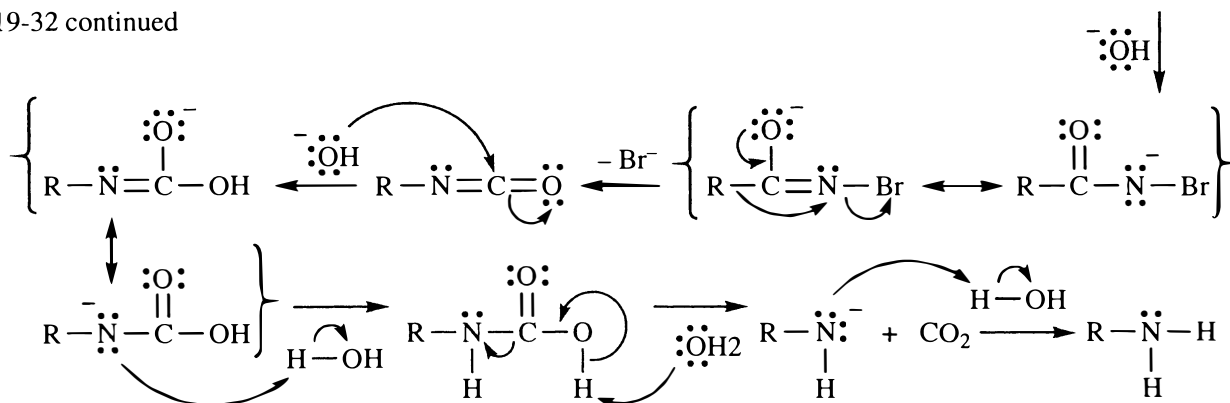
(b) 

(c) 

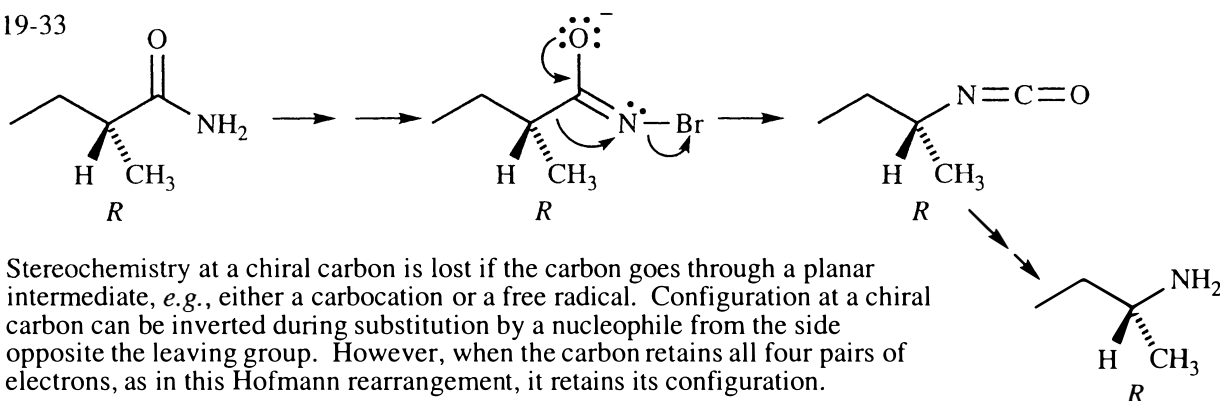
(d) 



19-32 continued



19-33

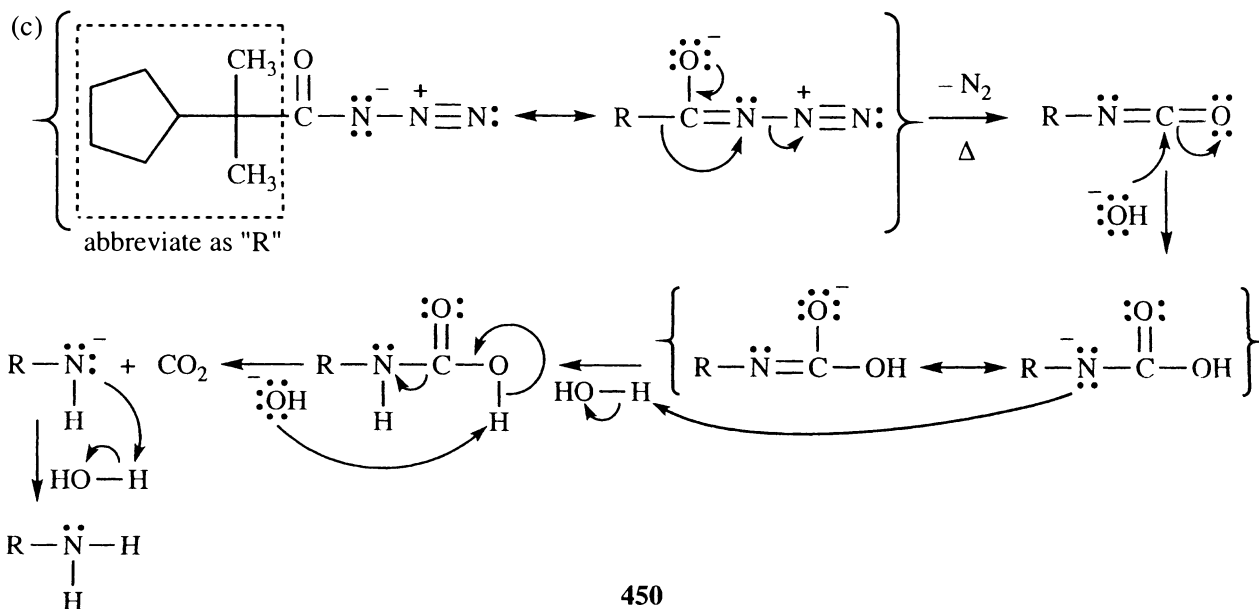


Stereochemistry at a chiral carbon is lost if the carbon goes through a planar intermediate, *e.g.*, either a carbocation or a free radical. Configuration at a chiral carbon can be inverted during substitution by a nucleophile from the side opposite the leaving group. However, when the carbon retains all four pairs of electrons, as in this Hofmann rearrangement, it retains its configuration.

19-34

(a) The acyl azide of the Curtius rearrangement is similar to the N-bromoamide of the Hofmann rearrangement in that both have an amide nitrogen with a good leaving group attached. Subsequent alkyl migration to the isocyanate and hydrolysis through the carbamic acid to the amine are identical in both mechanisms.

(b) The leaving group in the Curtius rearrangement is N_2 gas, one of the best leaving groups known "to man or beast", as we used to say.

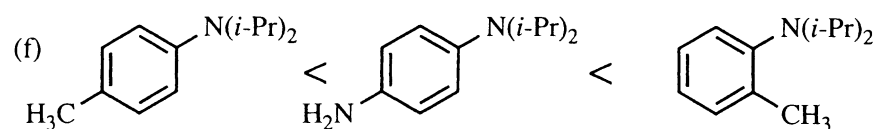
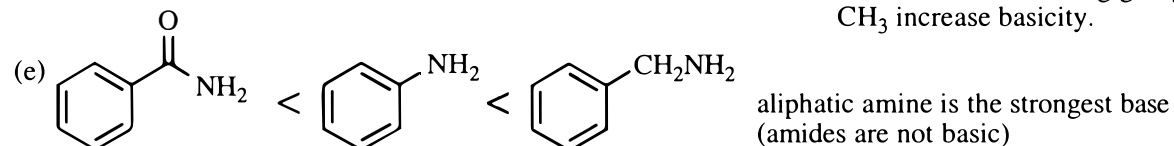
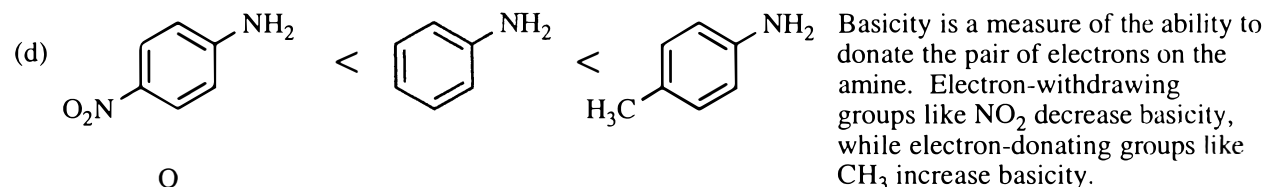
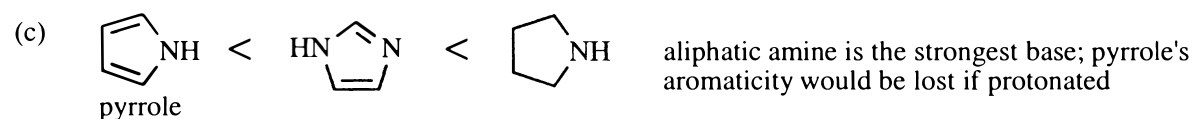
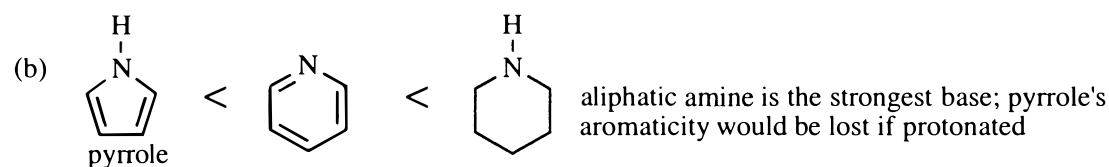
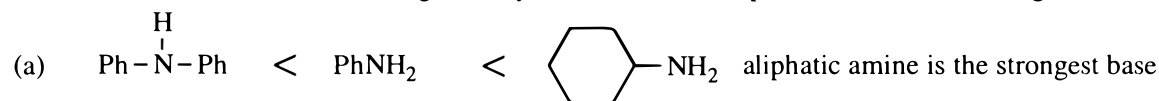


19-35 Please refer to solution 1-20, page 12 of this Solutions Manual.

19-36

- (a) primary amine; 2,2-dimethylpropan-1-amine, or neopentylamine
- (b) secondary amine; *N*-methylpropan-2-amine, or isopropylmethylamine
- (c) tertiary heterocyclic amine and a nitro group; 3-nitropyridine
- (d) quaternary heterocyclic ammonium ion; *N,N*-dimethylpiperidinium iodide
- (e) tertiary aromatic amine oxide; *N*-ethyl-*N*-methylaniline oxide
- (f) tertiary aromatic amine; *N*-ethyl-*N*-methylaniline
- (g) tertiary heterocyclic ammonium ion; pyridinium chloride
- (h) secondary amine; *N*,4-diethylhexan-3-amine

19-37 Shown in order of increasing basicity. In sets a-c, the aliphatic amine is the strongest base.



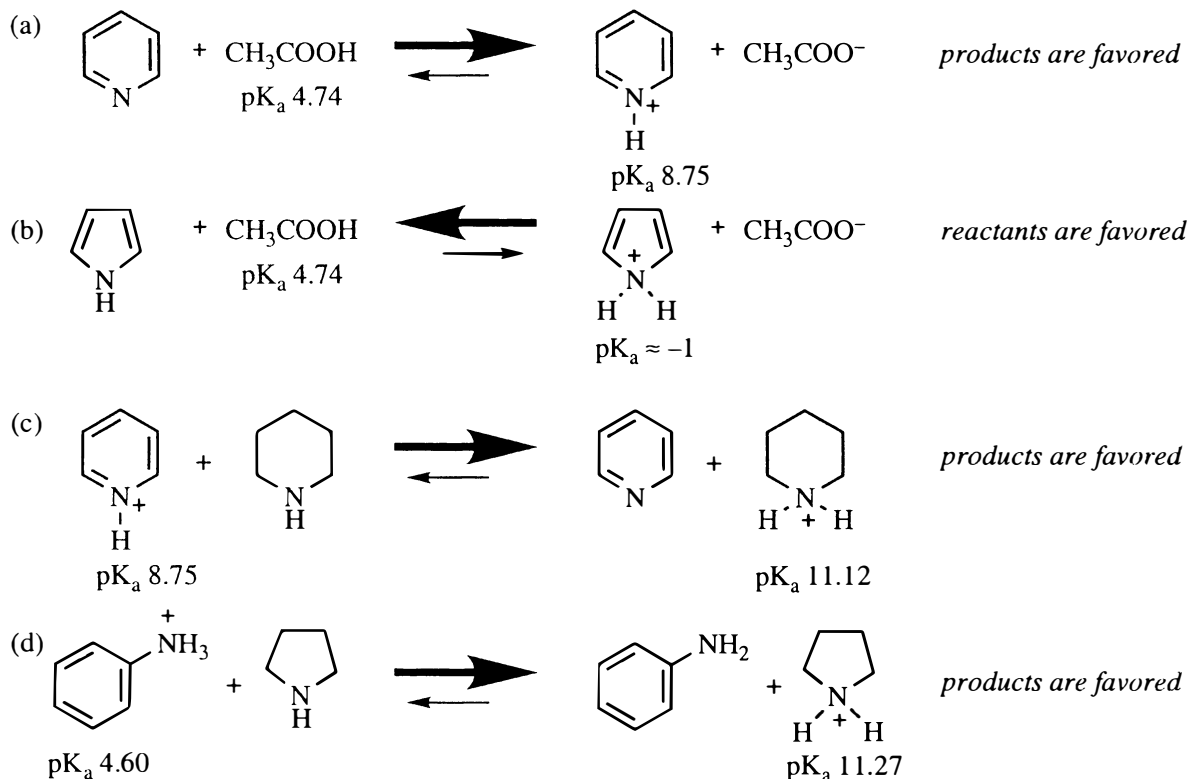
Congratulations if you got this one right! CH_3 is only slightly electron-donating by induction so the first structure puts the least electron density on the N. The second structure is more basic (by about 1 pK unit) because NH_2 is electron-donating by resonance. The last structure is the strongest base for a completely different reason: steric inhibition of resonance. (See the last topic in Appendix Two of this Manual.) The ortho methyl interferes with the isopropyl substituents on N and it forces the NR_2 out of planarity with the ring, so that the electron pair on the N is not conjugated with the aromatic pi system. Essentially, this N becomes an aliphatic amine. The pK_b of 2-methyl-*N,N*-diethylaniline is 6.9, about 2.5 pK units more basic than aniline. It is not as strong a base as a tertiary aliphatic amine because the aromatic ring is somewhat electron withdrawing by induction, yet the ortho methyl reduces the pi overlap of the nitrogen's electrons to make the N significantly more basic.

19-38

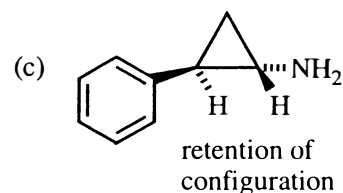
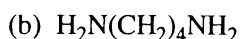
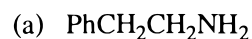
- (a) not resolvable: planar
 (c) not resolvable: symmetric
 (e) not resolvable: symmetric
 (g) not resolvable in conditions where the proton on N can exchange

- (b) resolvable: asymmetric carbon
 (d) resolvable: nitrogen inversion is very slow
 (f) resolvable: asymmetric nitrogen, unable to invert
 (h) resolvable: asymmetric nitrogen, unable to invert

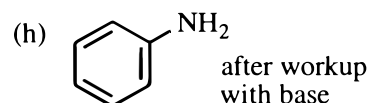
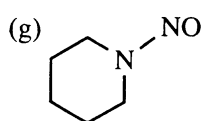
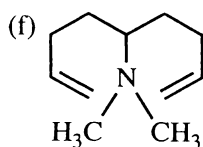
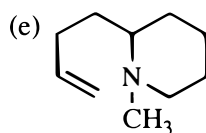
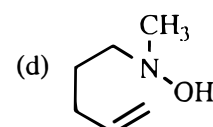
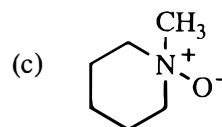
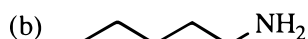
19-39 The values of pK_b of amines or pK_a of the conjugate acids can be obtained from Table 19-3. The side of the reaction with the weaker acid and base will be favored at equilibrium. (See Appendix 2 for a discussion of acidity and basicity.)



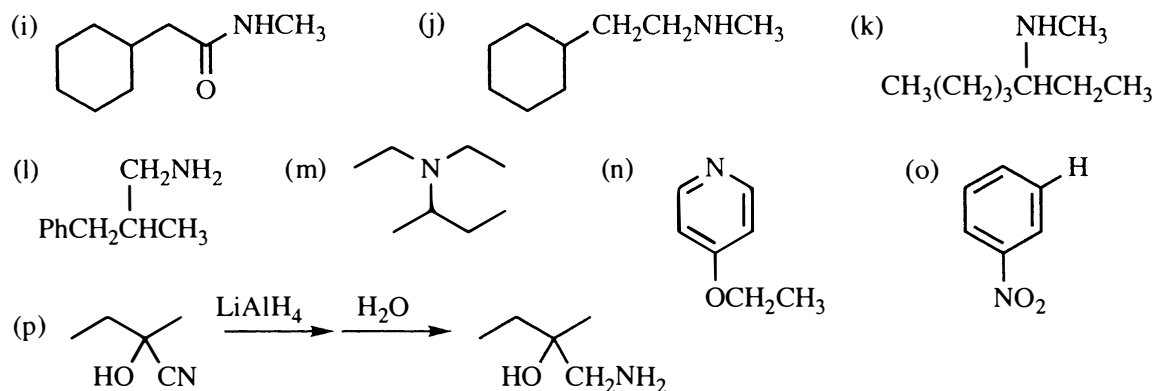
19-40



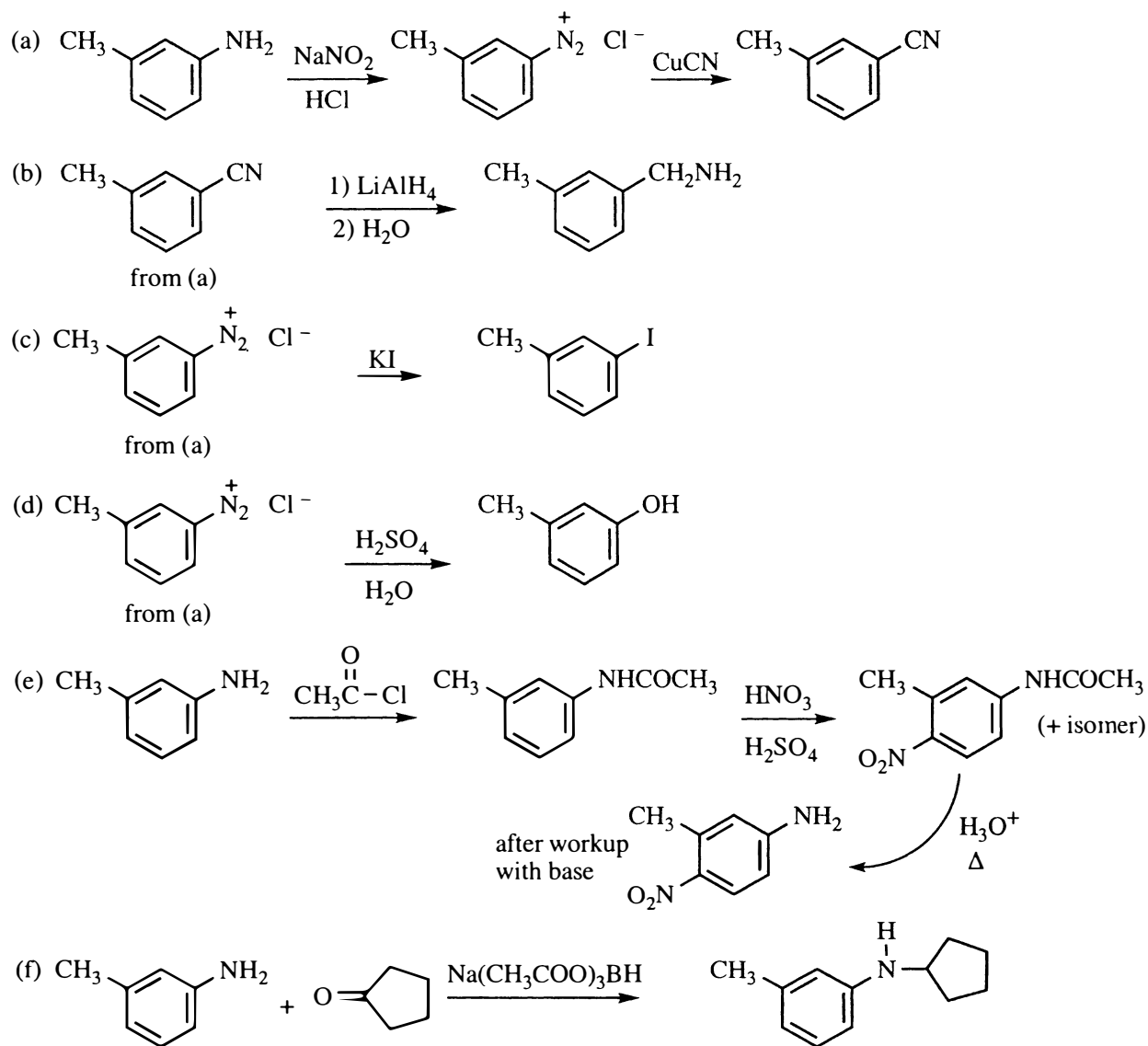
19-41



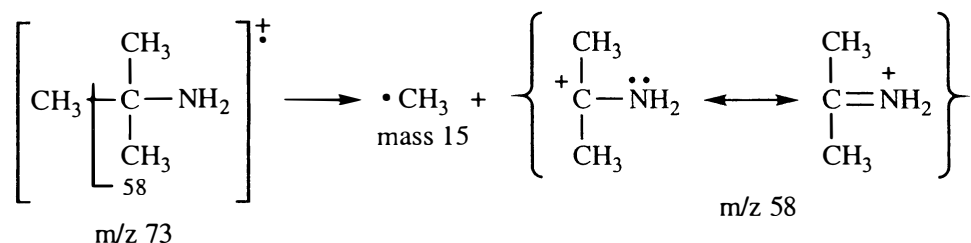
19-41 continued



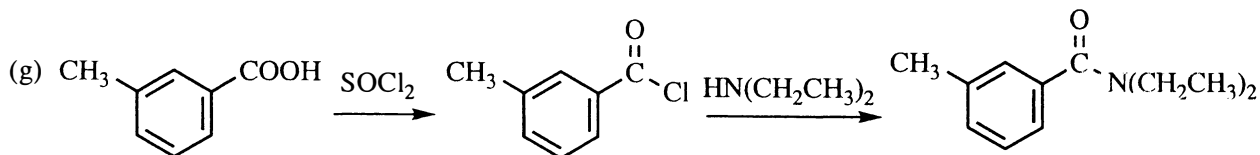
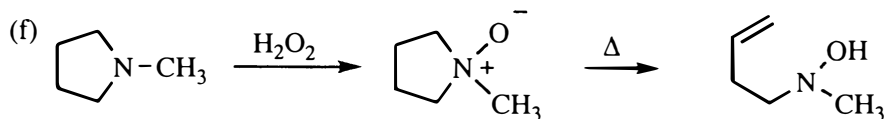
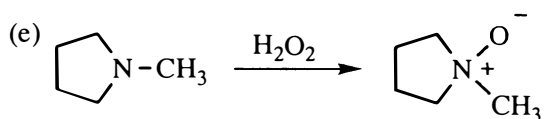
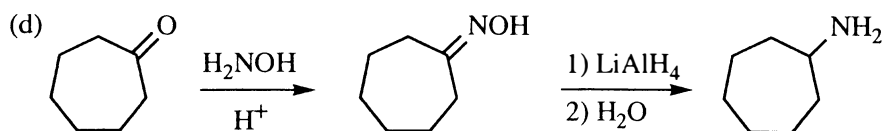
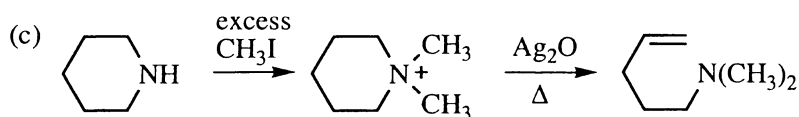
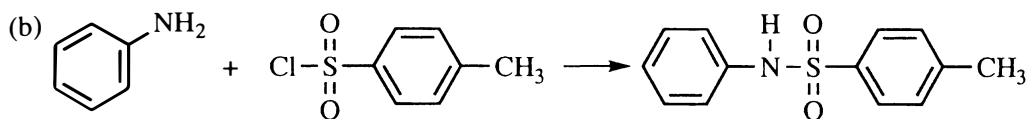
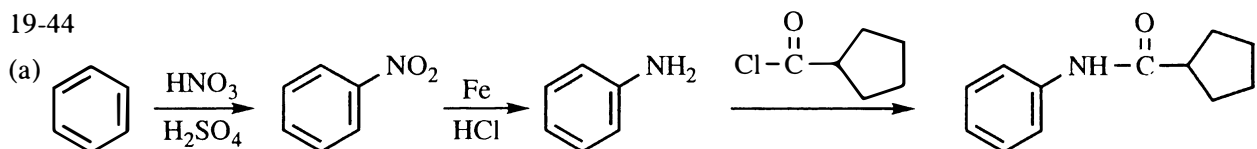
19-42



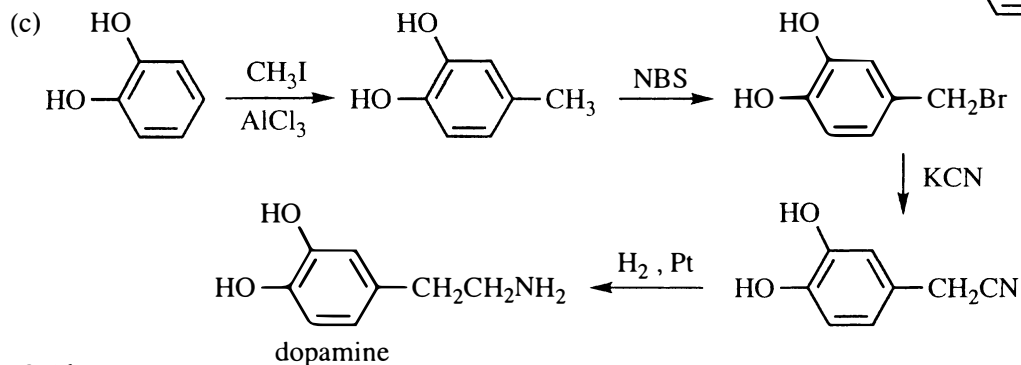
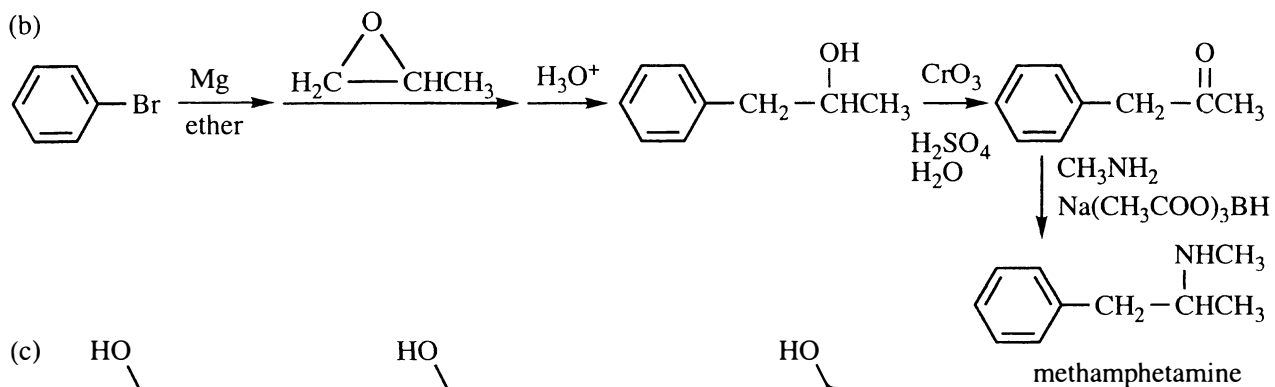
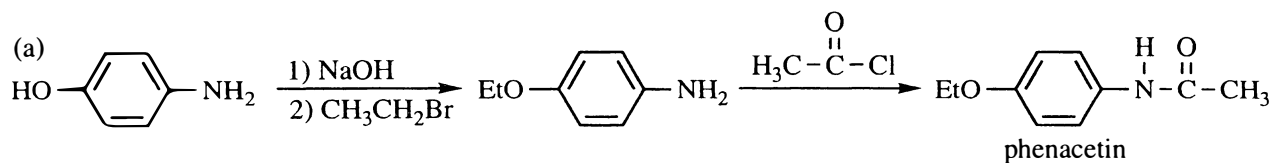
19-43 This fragmentation is favorable because the iminium ion produced is stabilized by resonance. Also, there are three possible cleavages that give the same ion. Both factors combine to make the cleavage facile, at the expense of the molecular ion.



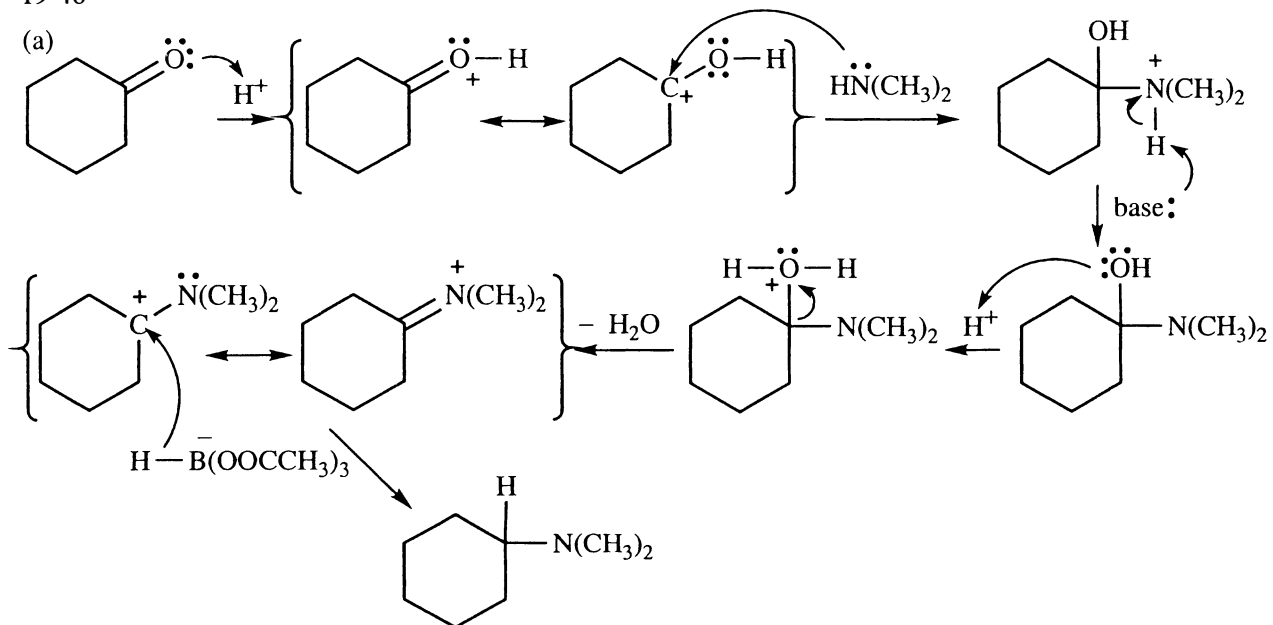
19-44



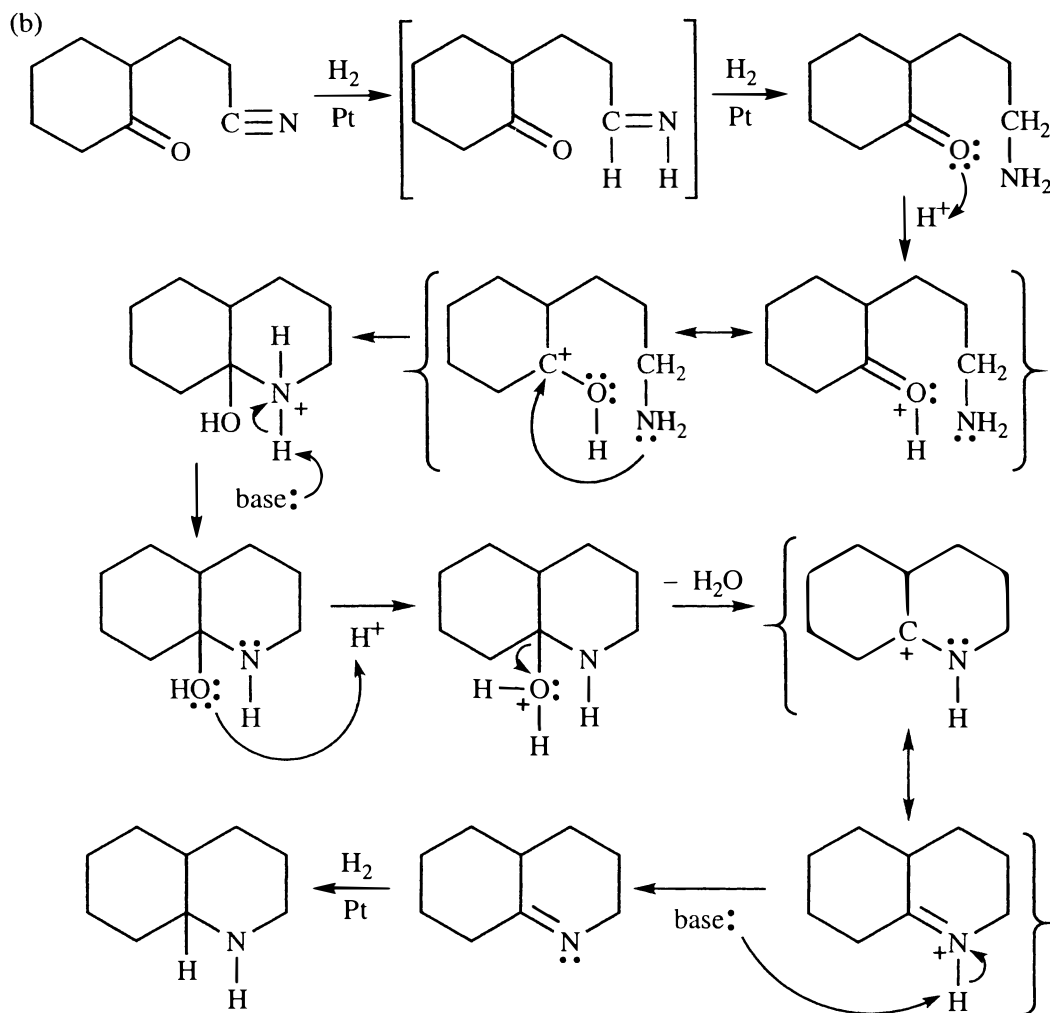
19-45 The problem restricts the starting materials to six carbons or fewer. Always choose starting materials with as many of the necessary functional groups as possible.



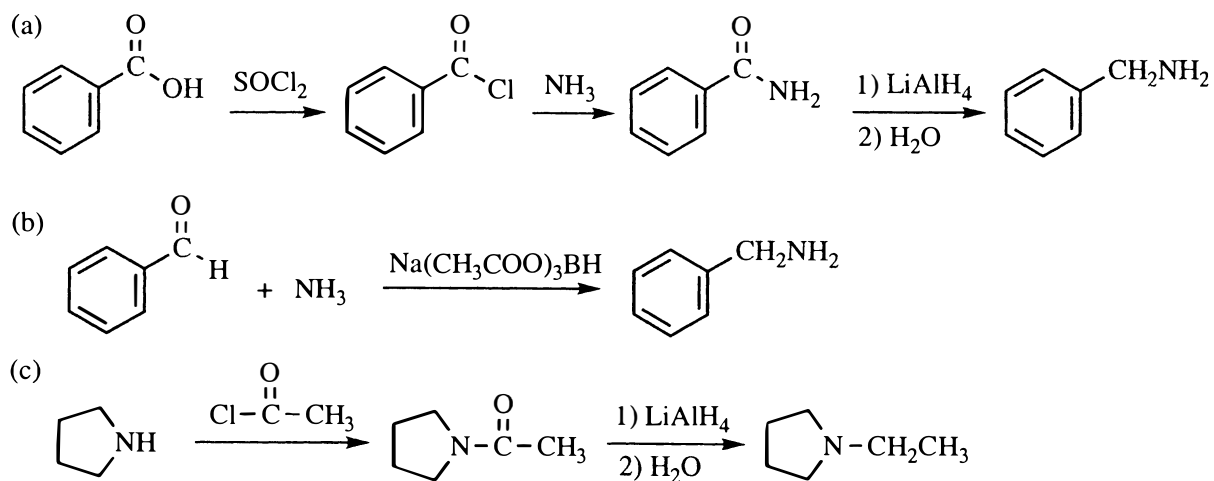
19-46



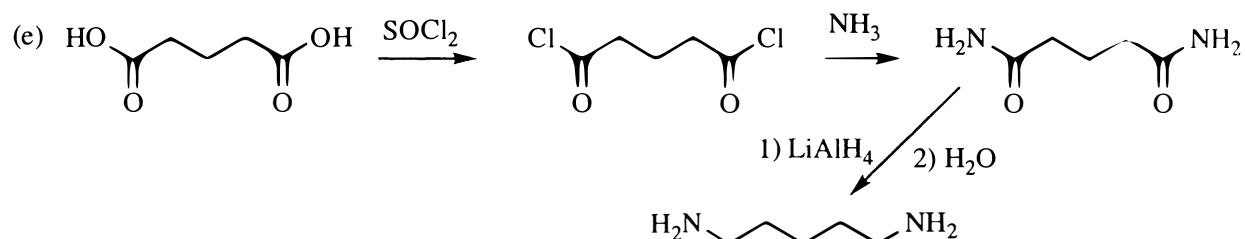
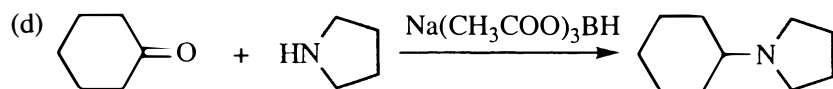
19-46 continued



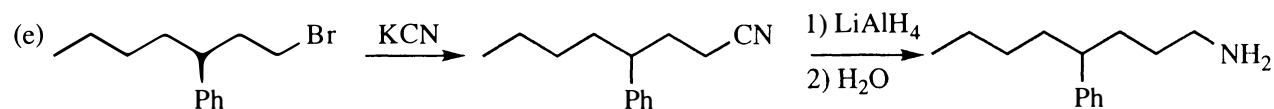
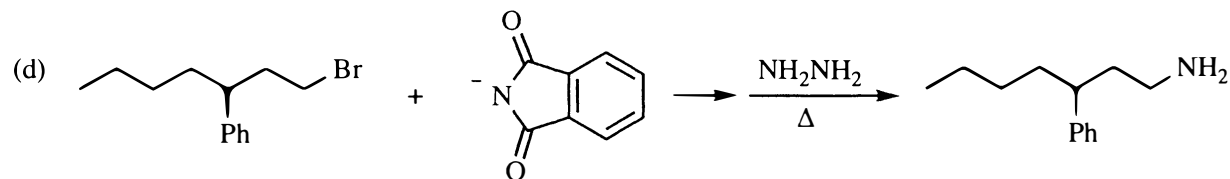
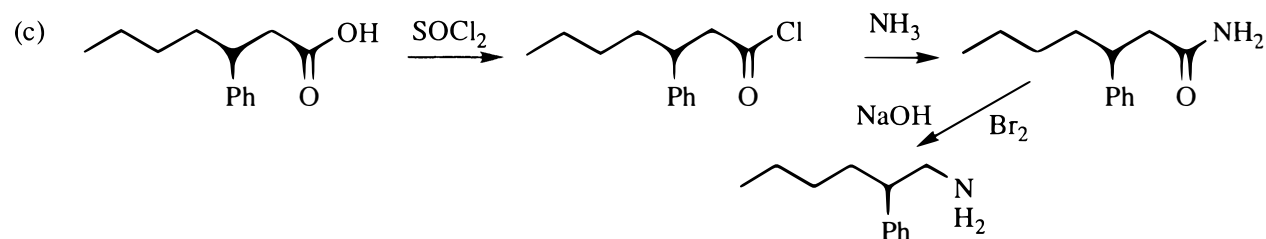
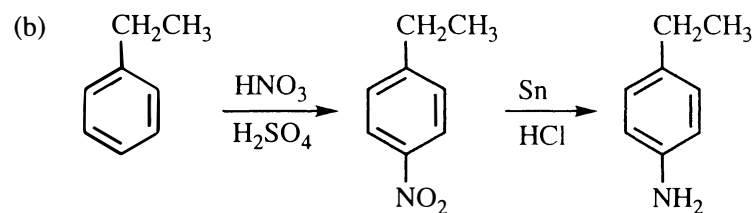
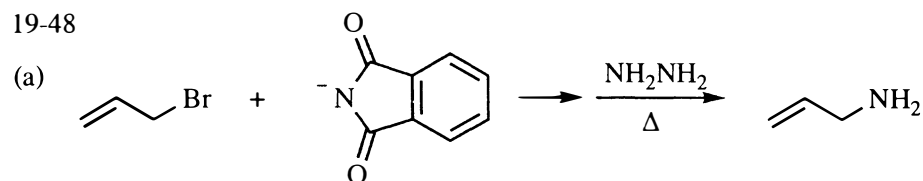
19-47



19-47 continued

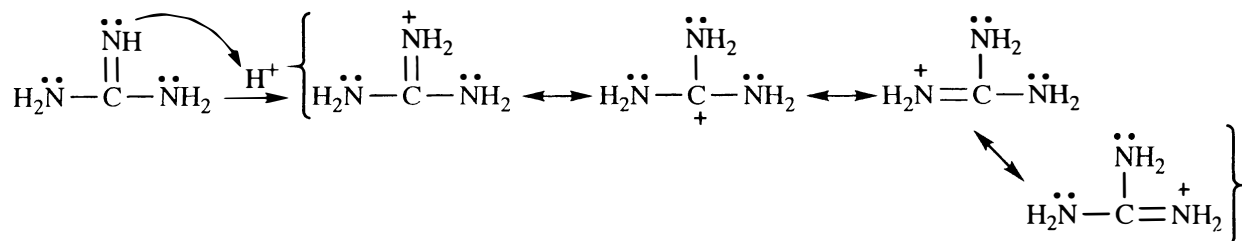


19-48

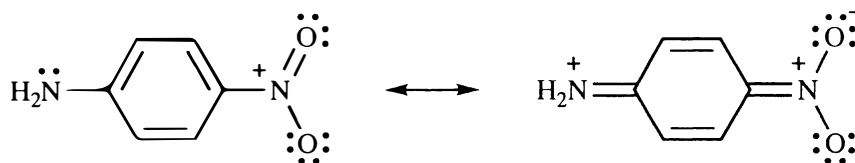


19-49

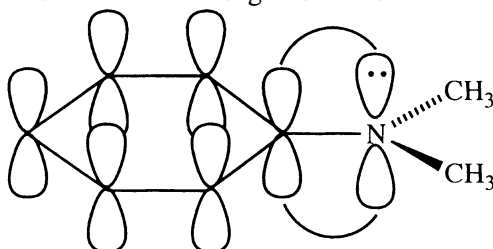
(a) When guanidine is protonated, the cation is greatly stabilized by resonance, distributing the positive charge over all atoms (except H):



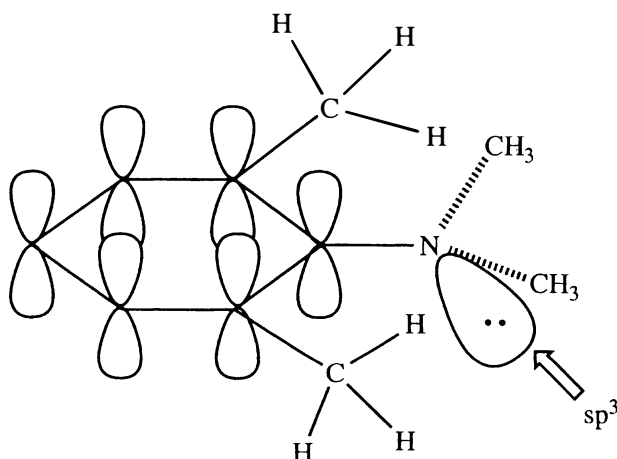
(b) The unprotonated molecule has a resonance form shown below that the protonated molecule cannot have. Therefore, the unprotonated form is stabilized relative to the protonated form. This greater stabilization of the unprotonated form is reflected in weaker basicity.



(c) Anilines are weaker bases than aliphatic amines because the electron pair on the nitrogen is shared with the ring, stabilizing the system. There is a steric requirement, however: the p orbital on the N must be parallel with the p orbitals on the benzene ring in order for the electrons on N to be distributed into the π system of the ring.

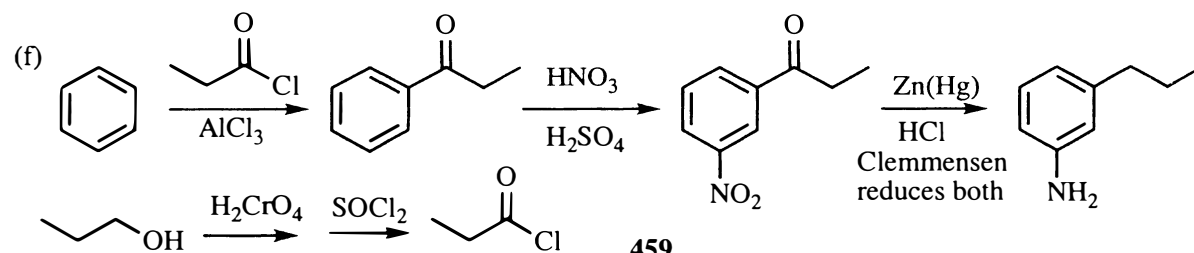
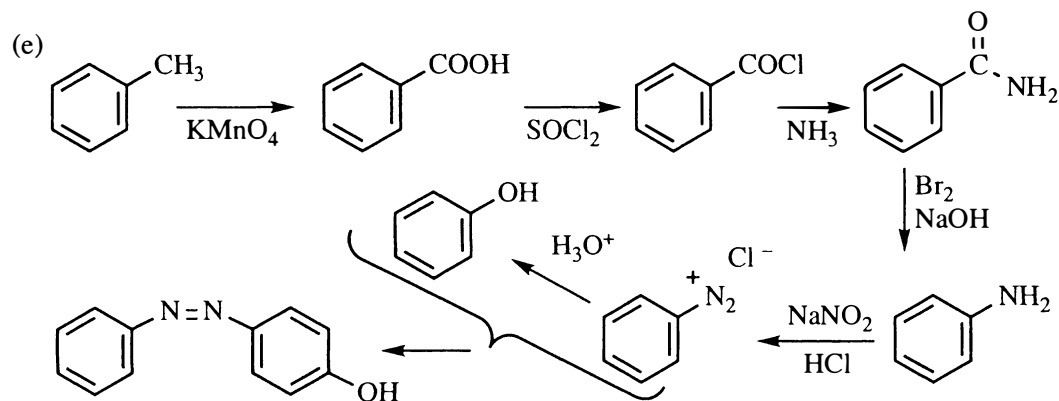
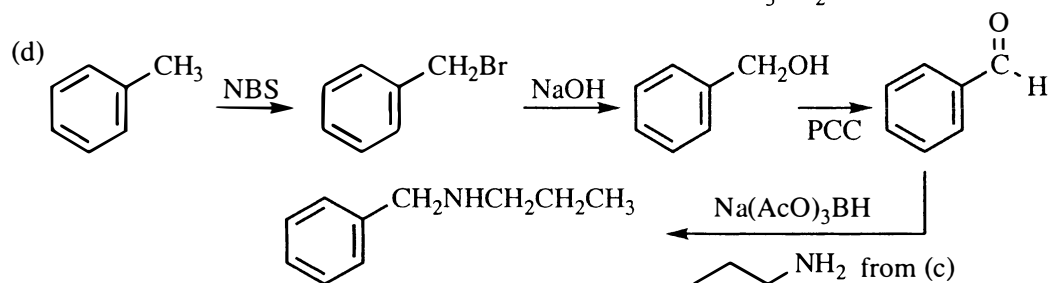
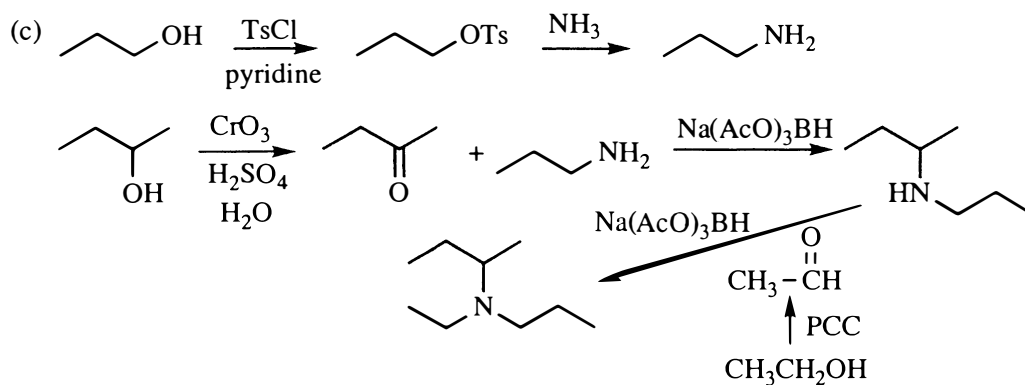
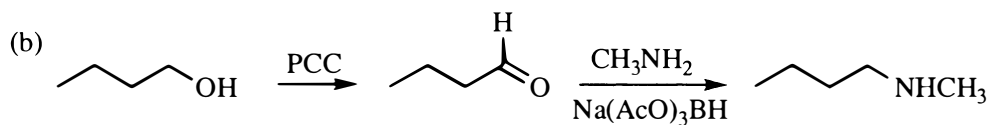


If the orbital on the nitrogen is forced out of this orientation (by substitution on C-2 and C-6, for example), the electrons are no longer shared with the ring. The nitrogen is hybridized sp^3 (no longer any reason to be sp^2), and the electron pair is readily available for bonding $\Rightarrow$ increased basicity.

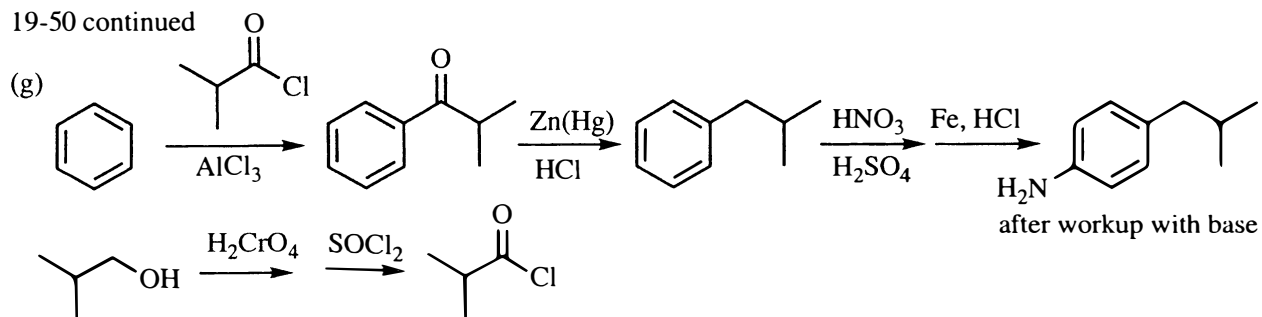


As surprising as it sounds, this aniline is about as basic as a tertiary aliphatic amine, except that the aromatic ring substituent is electron-withdrawing by induction, decreasing the basicity slightly. This phenomenon is called "steric inhibition of resonance". We will see more examples in future chapters. Also, it is the last topic in Appendix 2. (See another example in the solution to 19-37(f).)

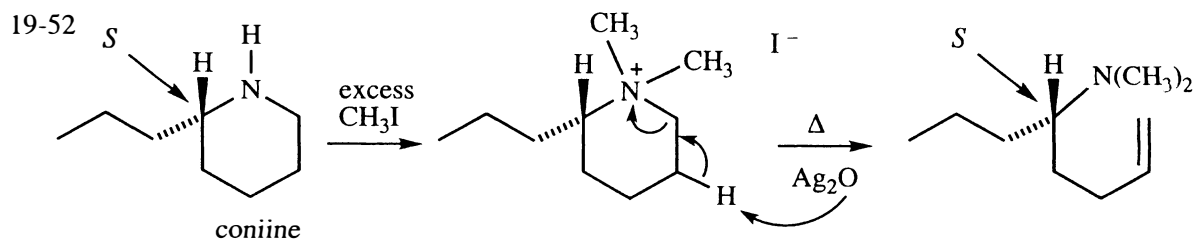
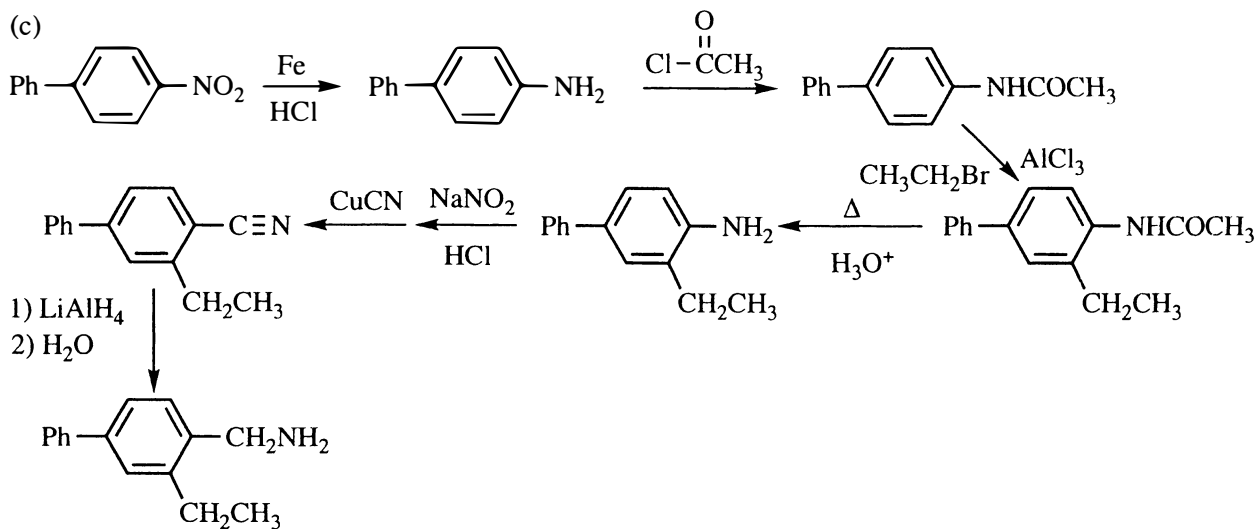
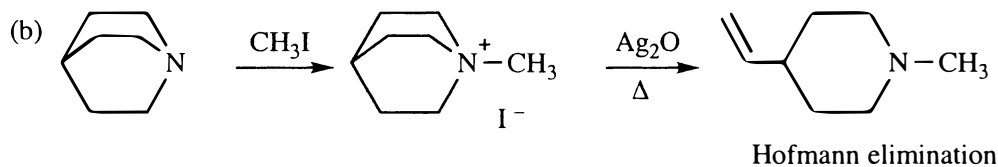
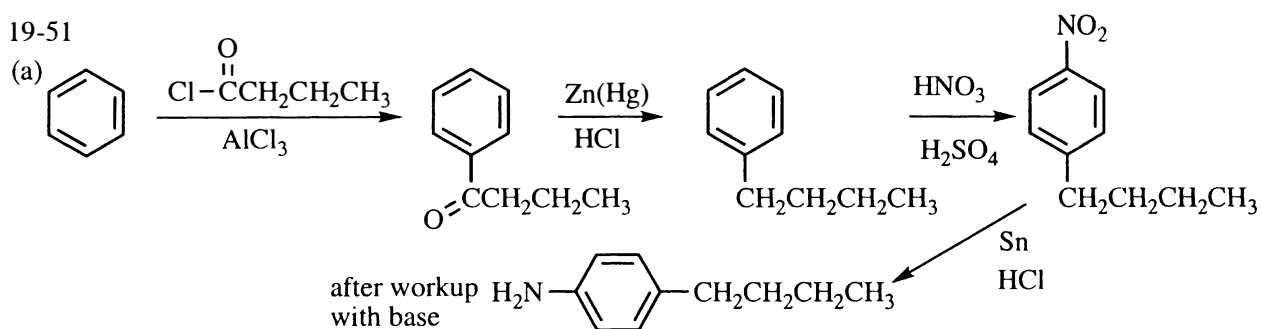
19-50 In this problem, sodium triacetoxyborohydride will be represented as $\text{Na}(\text{AcO})_3\text{BH}$.



19-50 continued



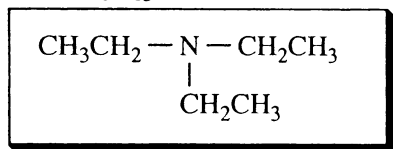
19-51



19-53

unknown X

(a)

—fishy odor $\Rightarrow$ amine—molecular weight 101 $\Rightarrow$ odd number of nitrogens $\Rightarrow$ if one nitrogen and no oxygen, the remainder is C_6H_{15} Mass spectrum:—fragment at 86 = $M - 15$ = loss of methyl $\Rightarrow$ the compound is likely tohave this structural piece: $CH_3 - \underset{\substack{| \\ \alpha\text{-cleavage}}}{C} - N$ IR spectrum:—no OH, no NH $\Rightarrow$ must be a 3° amine—no C=O or C=C or C $\equiv$ N or NO₂NMR spectrum:—only a triplet and quartet, integration about 3 : 2 $\Rightarrow$ ethyl group(s) onlyassemble the evidence: $C_6H_{15}N$, 3° amine, only ethyl in the NMR:

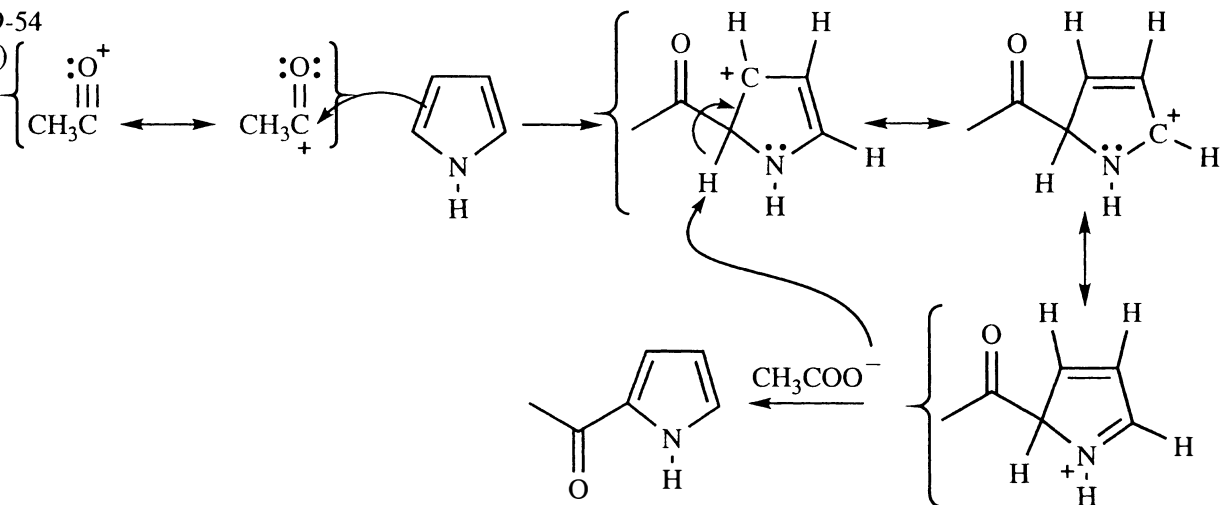
(b) React the triethylamine with HCl. The pure salt is solid and odorless.



(c) Washing her clothing in dilute acid like vinegar (dilute acetic acid) or dilute HCl would form a water-soluble salt as shown in (b). Normal washing will remove the water-soluble salt.

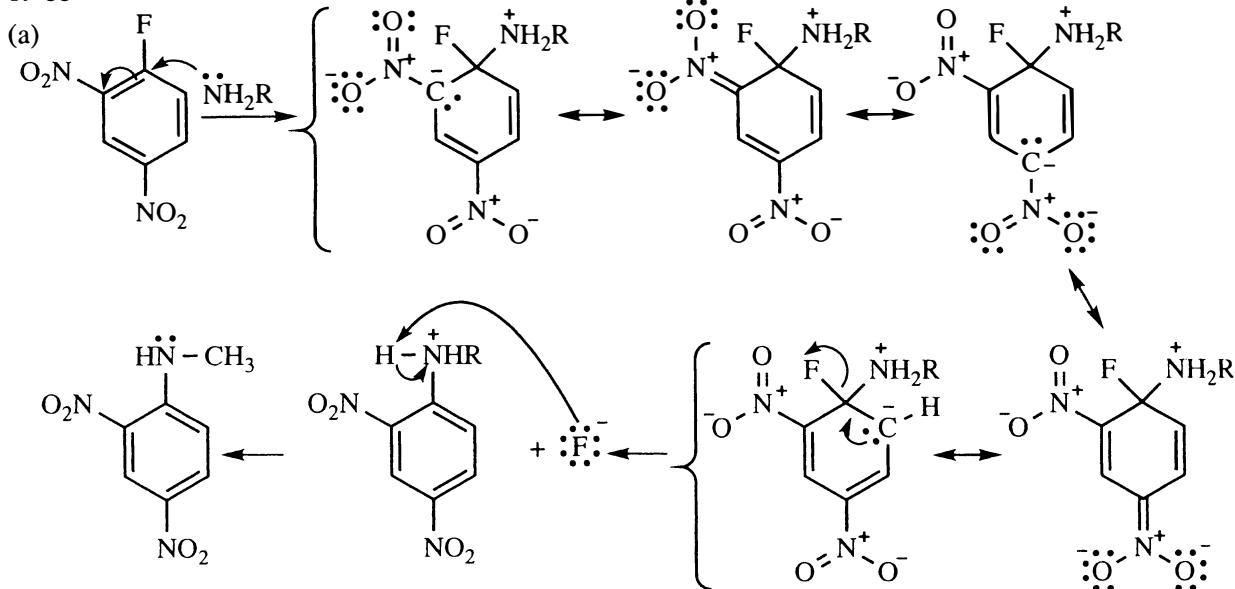
19-54

(a)

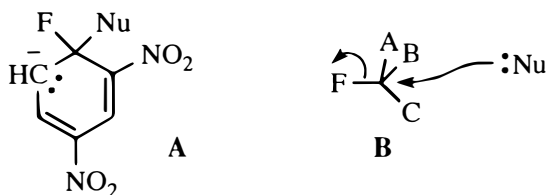


(b) Both answers can be found in the resonance forms of the intermediate, in particular, the resonance form that shows the positive charge on the N. This is the major resonance contributor; what is special about it is that every atom has a full octet, the best of all possible conditions. That does not arise in the benzene intermediate, so it must be easier to form the intermediate from pyrrole than from benzene. Also, acylation at the 3-position puts positive charge at the 2-position and on the N, but never on the other side of the ring, so this substitution has only two resonance forms. The intermediate from acylation at the 3-position is therefore not as stable as the intermediate from acylation at the 2-position.

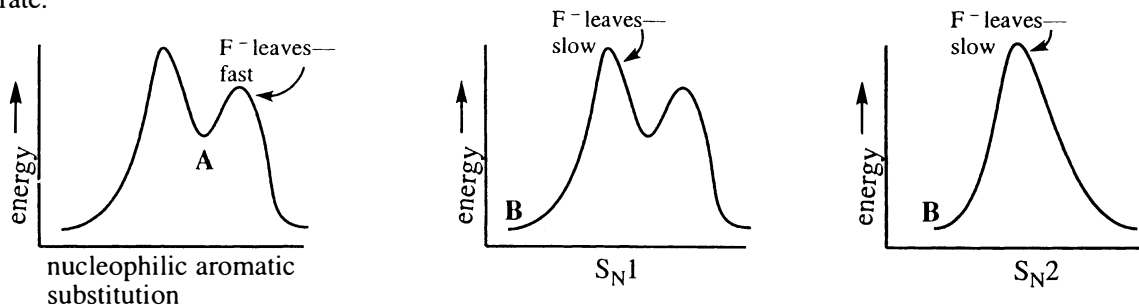
19-55



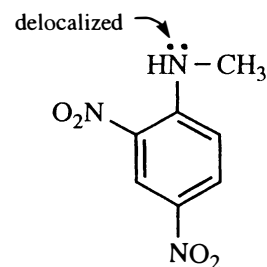
(b) Why is fluoride ion a good leaving group from **A** but not from **B** (either by S_N1 or S_N2)?



Formation of the anionic sigma complex **A** is the rate-determining (slow) step in nucleophilic aromatic substitution. The loss of fluoride ion occurs in a subsequent fast step where the nature of the leaving group does not affect the overall reaction rate. In the S_N1 or S_N2 mechanisms, however, the carbon-fluorine bond is breaking in the rate-determining step, so the poor leaving group ability of fluoride does indeed affect the rate.



(c) Amines can act as nucleophiles as long as the electron pair on the N is available for bonding. The initial reactant, methylamine, CH_3NH_2 , is a very reactive nucleophile. However, once the N is bonded to the benzene ring, the electron pair is delocalized onto the ring, especially with such strong electron-withdrawing groups like NO_2 in the ortho and para positions. The electrons on N are no longer available for bonding so there is no danger of it acting as a nucleophile in another reaction.



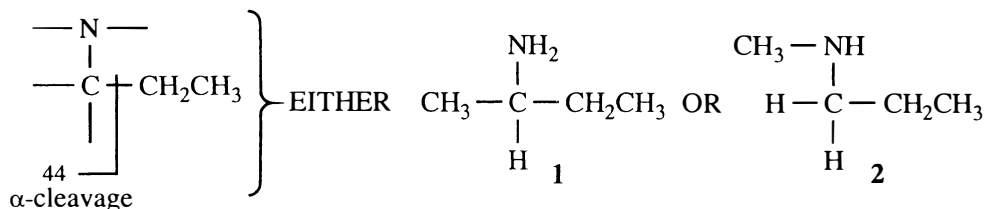
19-56 **Compound A**

Mass spectrum:

—molecular ion at 73 = odd mass = odd number of nitrogens;

if one nitrogen and no oxygen present $\Rightarrow$ molecular formula $C_4H_{11}N$

—base peak at 44 is $M - 29 \Rightarrow$ this fragment must be present:



IR spectrum:

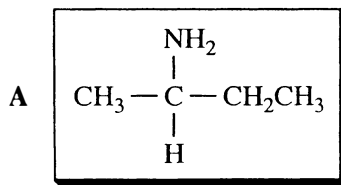
—two peaks around 3300 cm^{-1} indicate a 1° amine; no indication of oxygen

NMR spectrum:

—two exchangeable protons suggest NH_2 present

—1H multiplet at δ 2.8 means a CH—NH_2

The structure of **A** must be the same as **1** above:



Compound B

an isomer of **A**, so its molecular formula must also be $C_4H_{11}N$

IR spectrum:

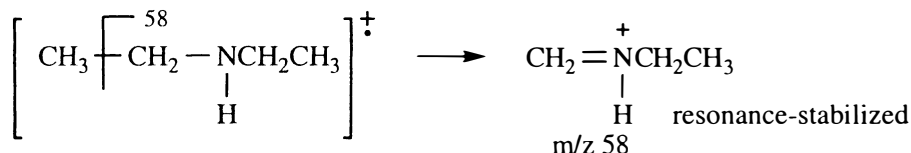
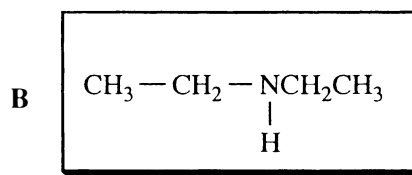
—only one peak at $3300\text{ cm}^{-1} \Rightarrow 2^\circ$ amine

NMR spectrum:

—one exchangeable proton $\Rightarrow \text{NH}$

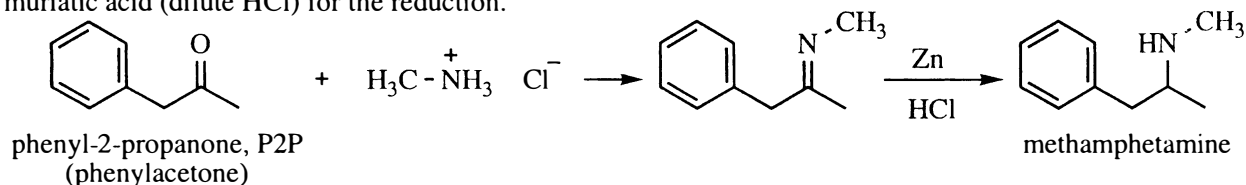
—two ethyls present

The structure of **B** must be:



19-57

(a) The acid-catalyzed condensation of P2P (a controlled substance) with methylamine hydrochloride gives an imine which can be reduced to methamphetamine. The suspect was probably planning to use zinc in muriatic acid (dilute HCl) for the reduction.

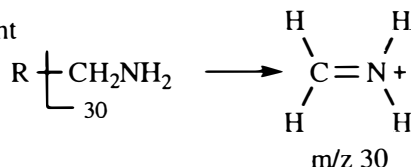


(b) The jury acquitted the defendant on the charge of attempted manufacture of methamphetamine. There were legal problems with possible entrapment, plus the fact that he had never opened the bottle of the starting material. The defendant was convicted on several possession charges, however, and was awarded four years of institutional time to study organic chemistry.

19-58

Mass spectrum:

- molecular ion at 87 = odd mass = odd number of nitrogens present
- if one nitrogen and no oxygens $\Rightarrow$ molecular formula $C_5H_{13}N$
- base peak at m/z 30 $\Rightarrow$ structure must include this fragment

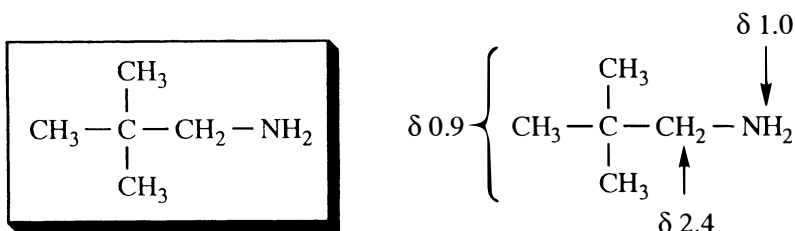


IR spectrum:

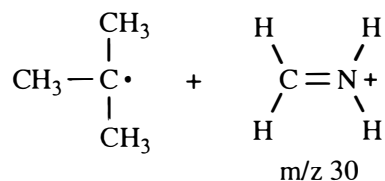
- two peaks in the $3300-3400\text{ cm}^{-1}$ region $\Rightarrow$ 1° amine

NMR spectrum:

- singlet at δ 0.9 for 9H must be a *t*-butyl group
- 2H signal at δ 1.0 exchanges with D_2O $\Rightarrow$ must be protons on N or O



Note that the base peak in the MS arises from cleavage to give these two, relatively stable fragments:



19-59 (a tough problem)

molecular formula $C_{11}H_{16}N_2$ has 5 elements of unsaturation, enough for a benzene ring; no oxygens precludes NO_2 and amide; if $C \equiv N$ is present, there are not enough elements of unsaturation left for a benzene ring, so benzene and $C \equiv N$ are mutually exclusive

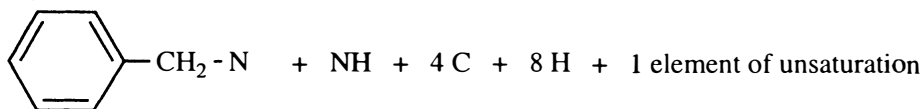
IR spectrum:

- one spike around 3300 cm^{-1} suggests a 2° amine
- no $C \equiv N$
- CH and C=C regions suggest an aromatic ring

Proton NMR spectrum:

- 5H multiplet at δ 7.3 indicates a monosubstituted benzene ring (the fact that all the peaks are huddled around 7.3 precludes N being bonded to the ring)
- 1H singlet at δ 2.0 is exchangeable $\Rightarrow$ NH of secondary amine
- 2H singlet at δ 3.5 is CH_2 ; the fact that it is so strongly deshielded and unsplit suggests that it is between a nitrogen and the benzene ring

fragments so far:



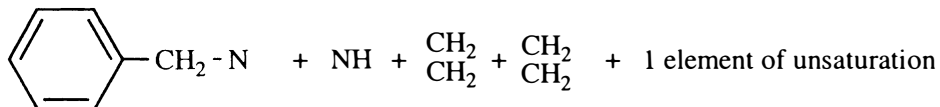
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19-59 continued

Carbon NMR spectrum:

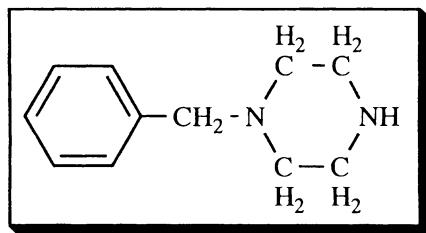
- four signals around δ 125-138 are the aromatic carbons
- the signal at δ 65 is the CH_2 bonded to the benzene
- the other 4 carbons come as two signals at δ 46 and δ 55; each is a triplet, so there are two sets of two equivalent CH_2 groups, each bonded to N to shift it downfield

fragments so far:



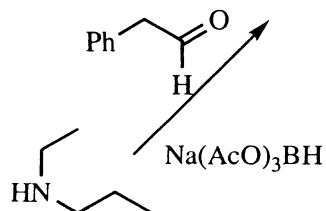
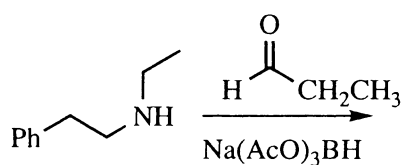
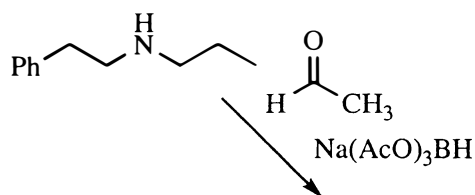
There is no evidence for an alkene in any of the spectra, so the remaining element of unsaturation must be a ring. The simplicity of the NMR spectra indicates a fairly symmetric compound.

Assemble the pieces:

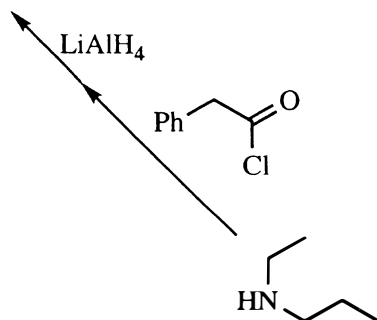
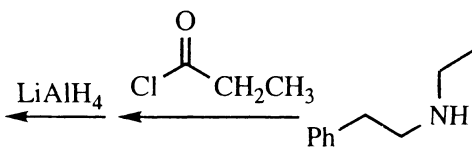
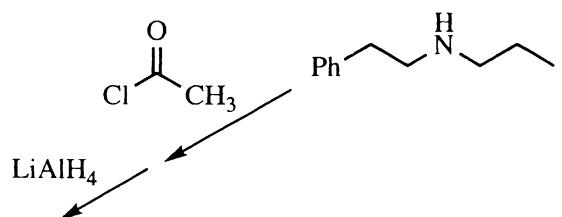


19-60

(a)

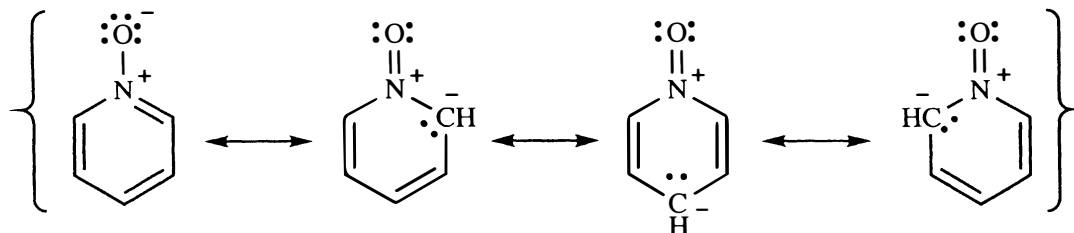


(b)



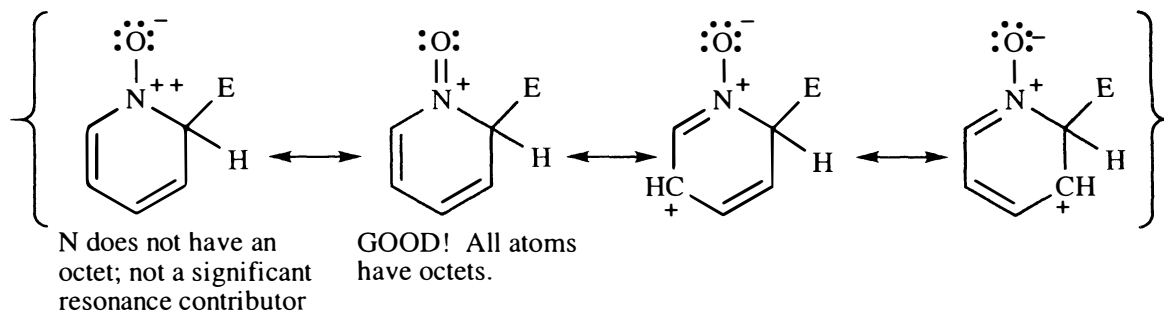
19-61 Not only is substitution at C-2 and C-4 the major products, but substitution occurs under surprisingly mild conditions.

Begin by drawing the resonance forms of pyridine N-oxide:

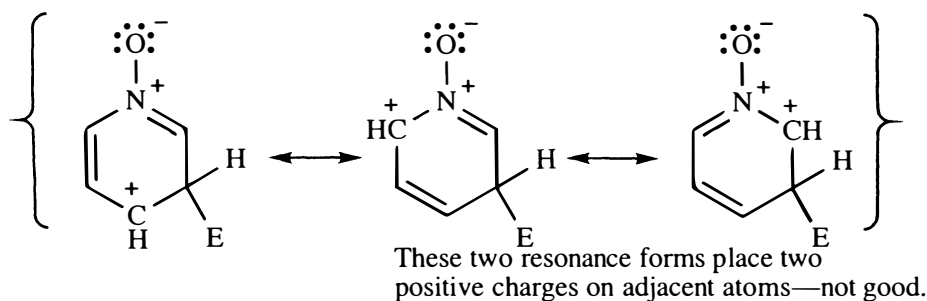


Resonance forms show that the electron density from the oxygen is distributed at C-2 and C-4; these positions would be the likely places for an electrophile to attack.

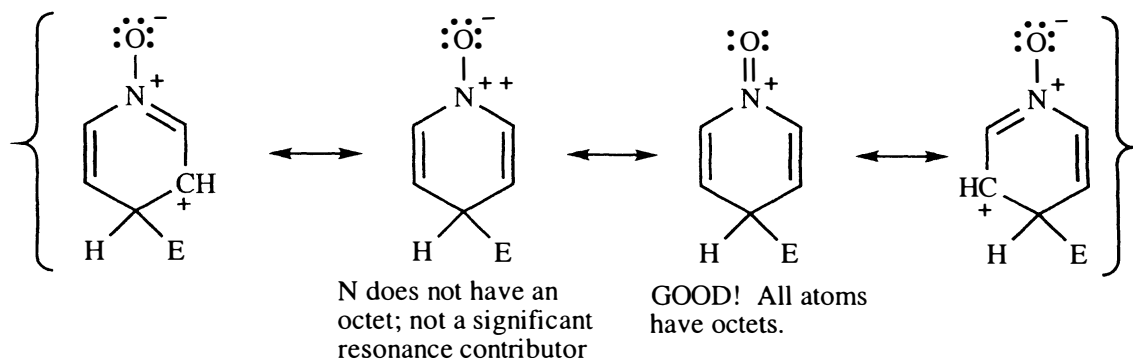
Resonance forms from electrophilic attack at C-2



Resonance forms from electrophilic attack at C-3



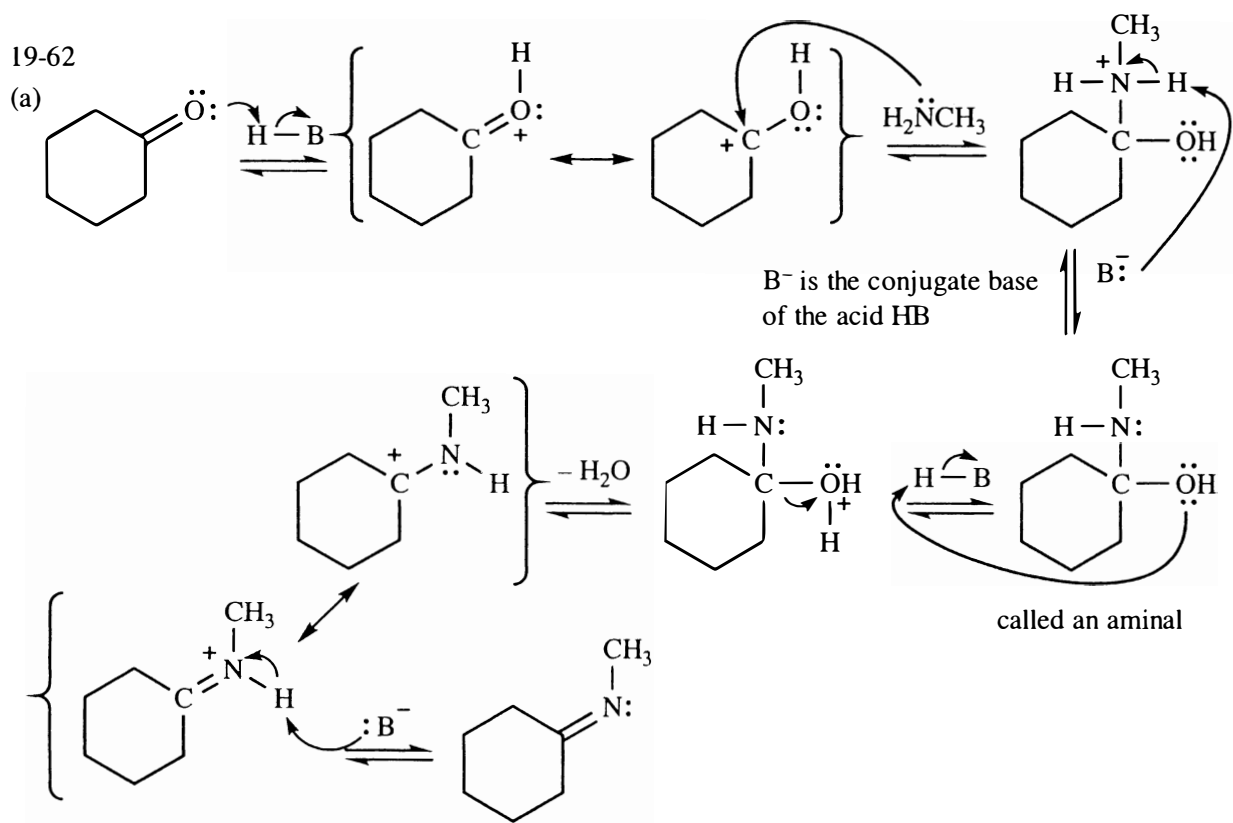
Resonance forms from electrophilic attack at C-4



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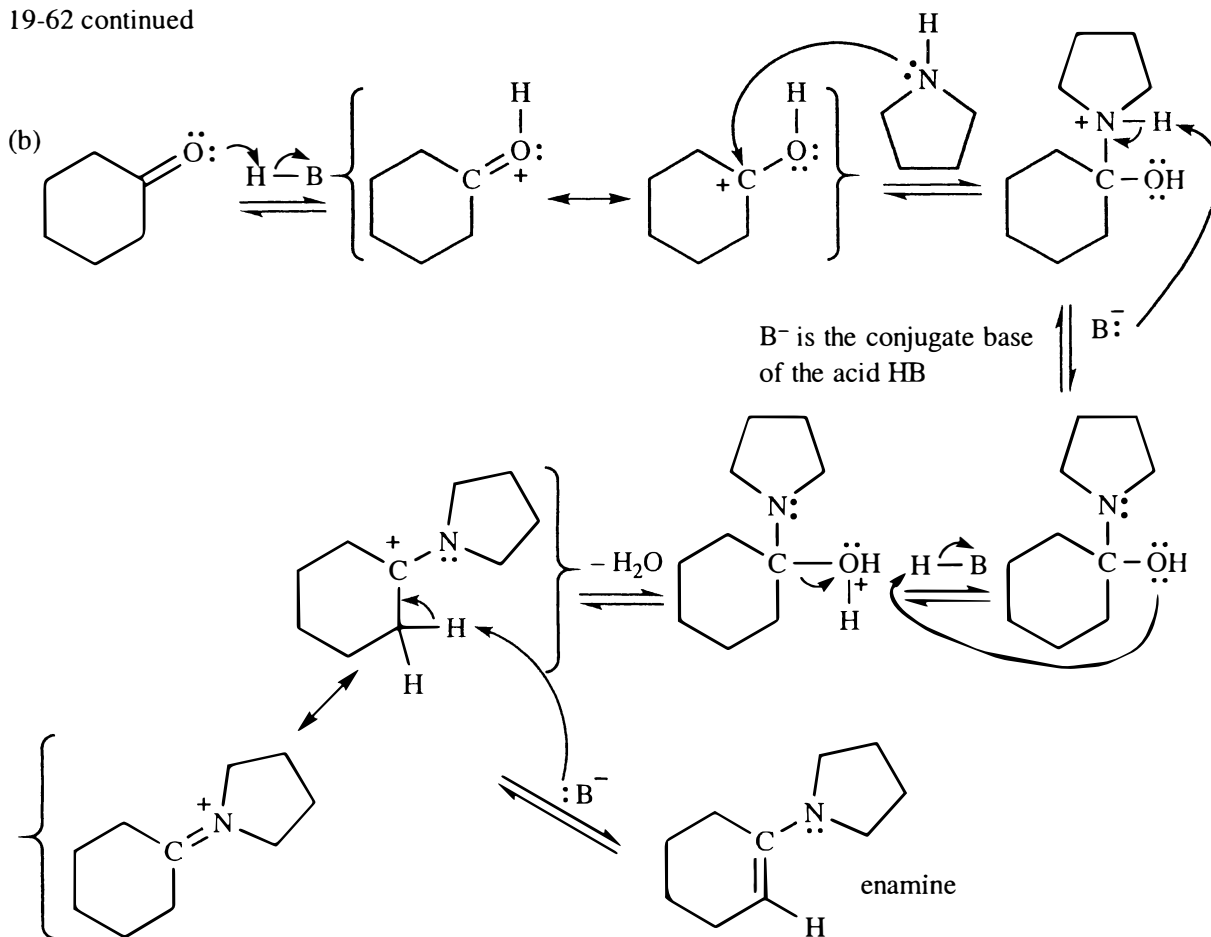
19-61 continued

The resonance forms from electrophilic attack at C-3 are bad; only one of the three is a significant contributor, which means that there is not much resonance stabilization. When the electrophile attacks at C-2 or C-4, however, there are two forms that are good plus one great one that has all atoms with full octets. Clearly, attack at C-2 and C-4 give the most stable intermediates and will be the preferred sites of attack.



continued on next page

19-62 continued

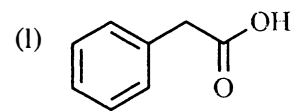
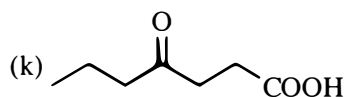
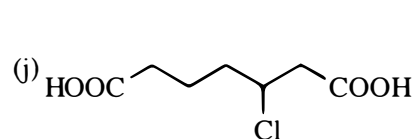
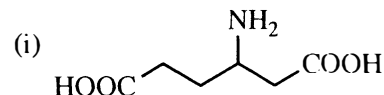
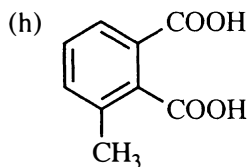
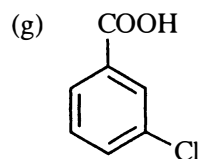
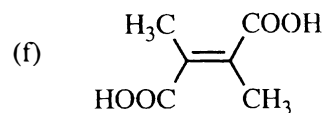
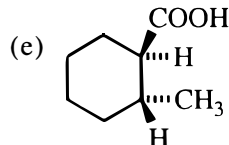
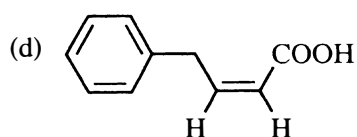
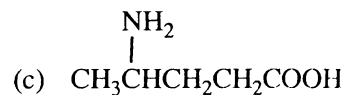
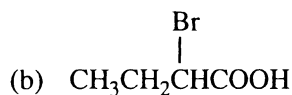
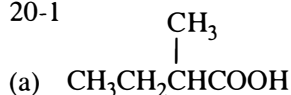


To this point, everything is the same in the two mechanisms.
But now, there is no H on the N to remove to form the imine.
The only H that can be removed to form a neutral intermediate
is the H on C next to the carbocation.

(c) A secondary amine has only one H to give which it loses in the first half of the mechanism to form the neutral intermediate called an aminal, equivalent to a hemiacetal. In the second half of the mechanism, the H on an adjacent carbon is removed to form the neutral product, the enamine. The type of product depends entirely on whether the amine begins with one or two hydrogen atoms.

CHAPTER 20—CARBOXYLIC ACIDS

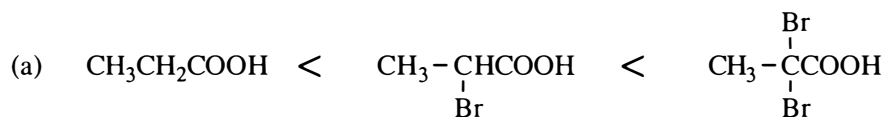
20-1



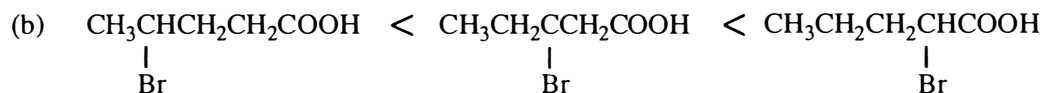
20-2 IUPAC name first; then common name.

- (a) 2-iodo-3-methylpentanoic acid; α -iodo- β -methylvaleric acid
 (b) (Z)-3,4-dimethylhex-3-enoic acid
 (c) 2,3-dinitrobenzoic acid; no common name
 (d) *trans*-cyclohexane-1,2-dicarboxylic acid; (*trans*-hexahydrophthalic acid)
 (e) 2-chlorobenzene-1,4-dicarboxylic acid; 2-chloroterephthalic acid
 (f) 3-methylhexanedioic acid; β -methyladipic acid

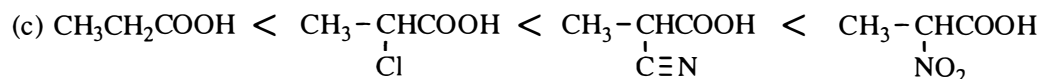
20-3 Listed in order of increasing acid strength (weakest acid first). (See Appendix 2 for a review of acidity.)



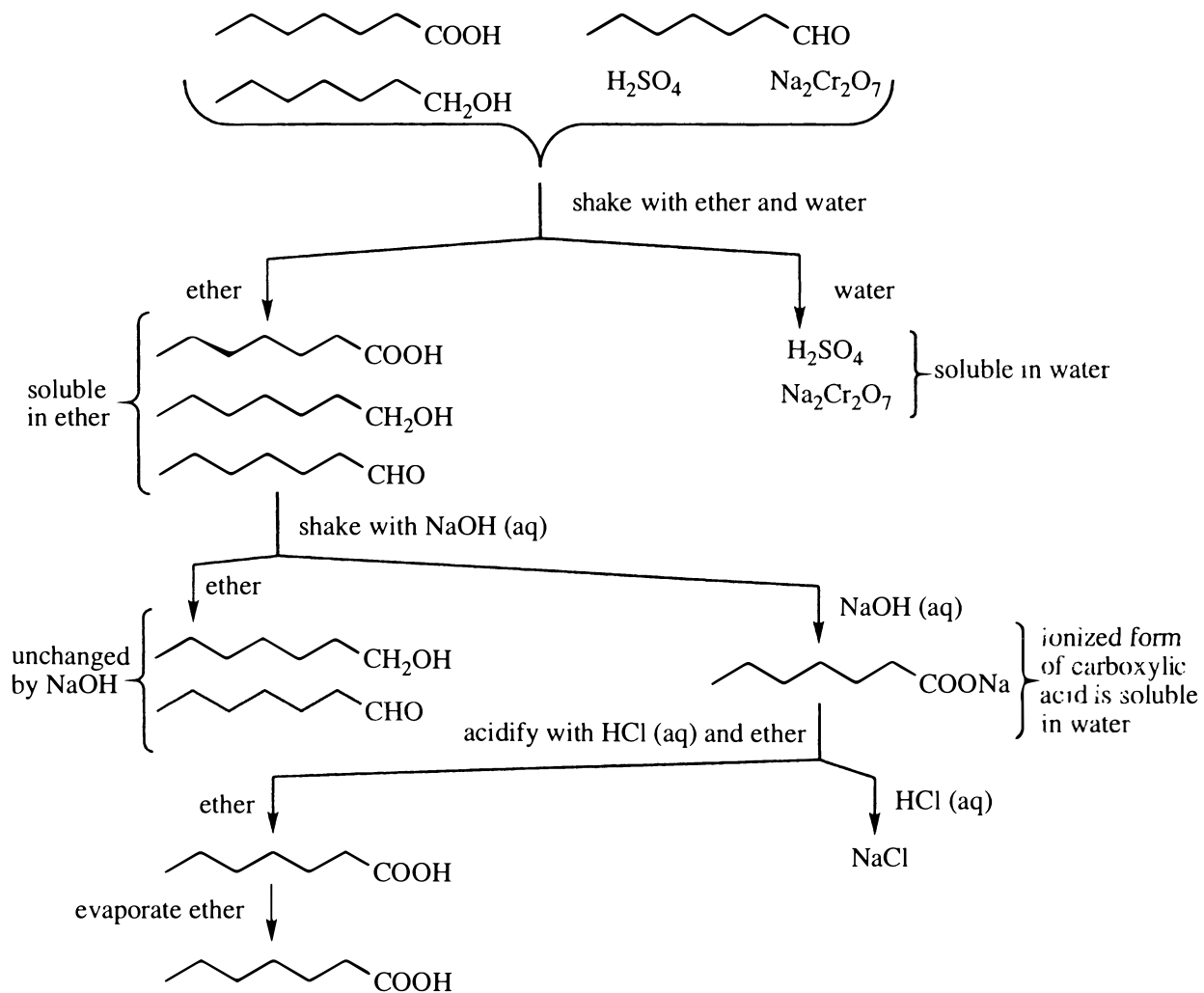
The greater the number of electron-withdrawing substituents, the greater the stabilization of the carboxylate ion.



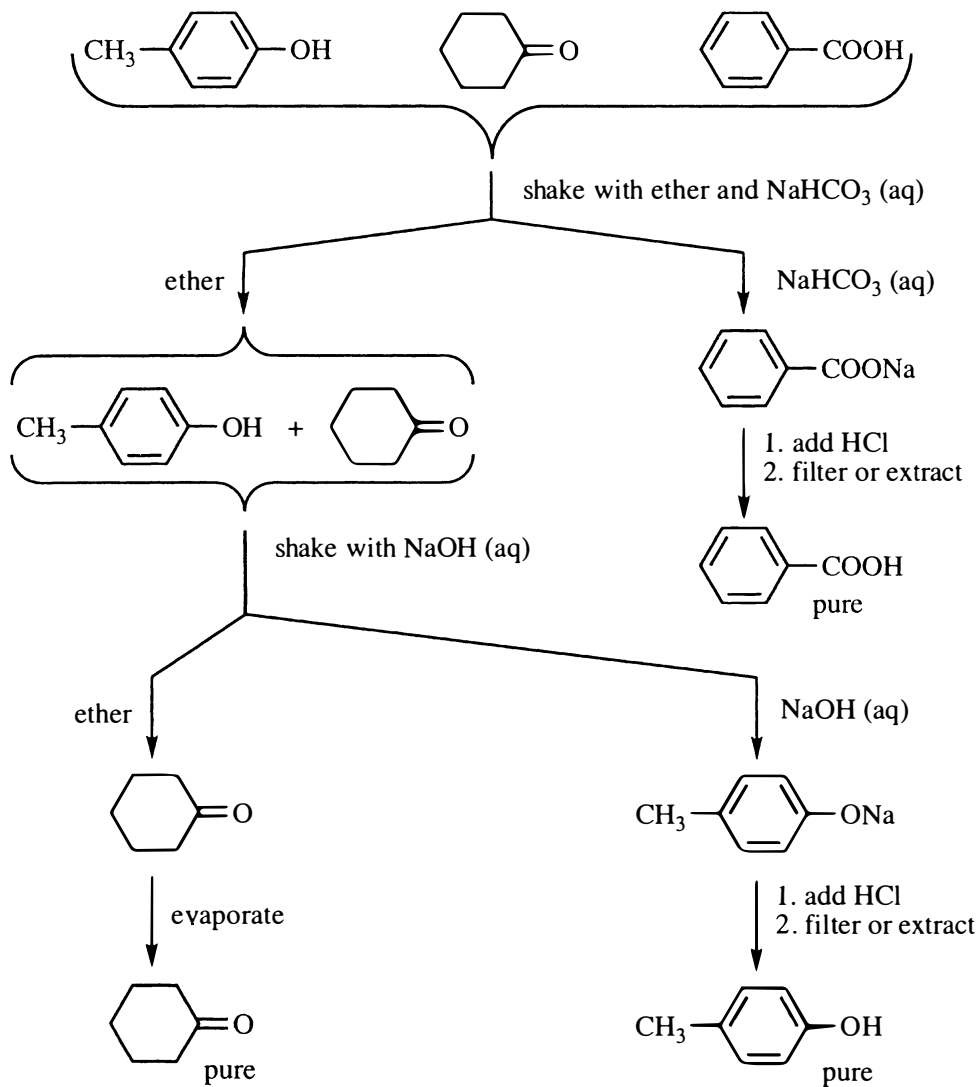
The closer the electron-withdrawing group, the greater the stabilization of the carboxylate ion.



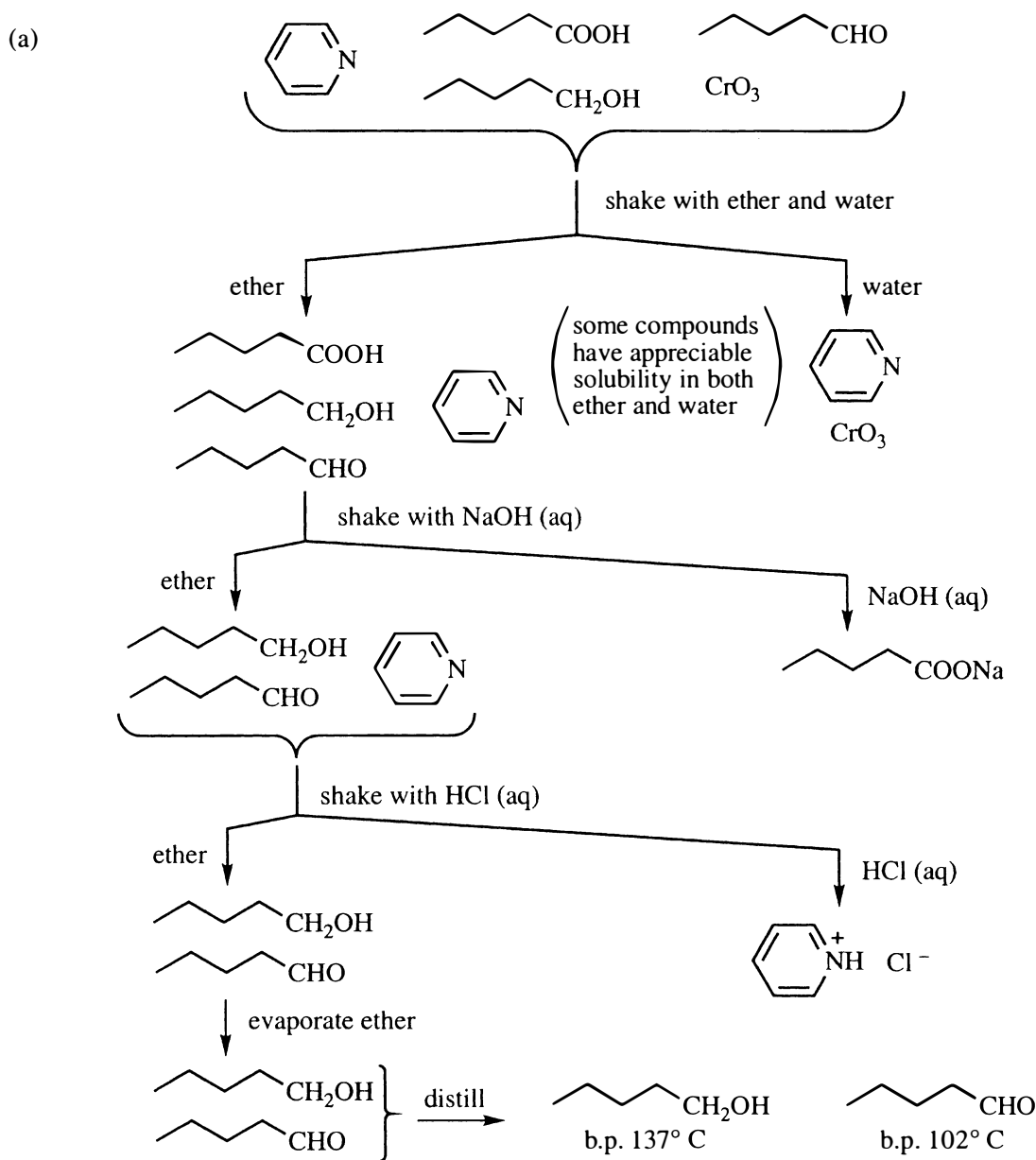
The stronger the electron-withdrawing effect of the substituent, the greater the stabilization of the carboxylate ion.



20-5 The principle used to separate a carboxylic acid (a stronger acid) from a phenol (a weaker acid) is to neutralize with a weak base (NaHCO_3), a base strong enough to ionize the stronger acid but not strong enough to ionize the weaker acid.



20-6 The reaction mixture includes the initial reactant, reagent, desired product, and the overoxidation product—not unusual for an organic reaction mixture.

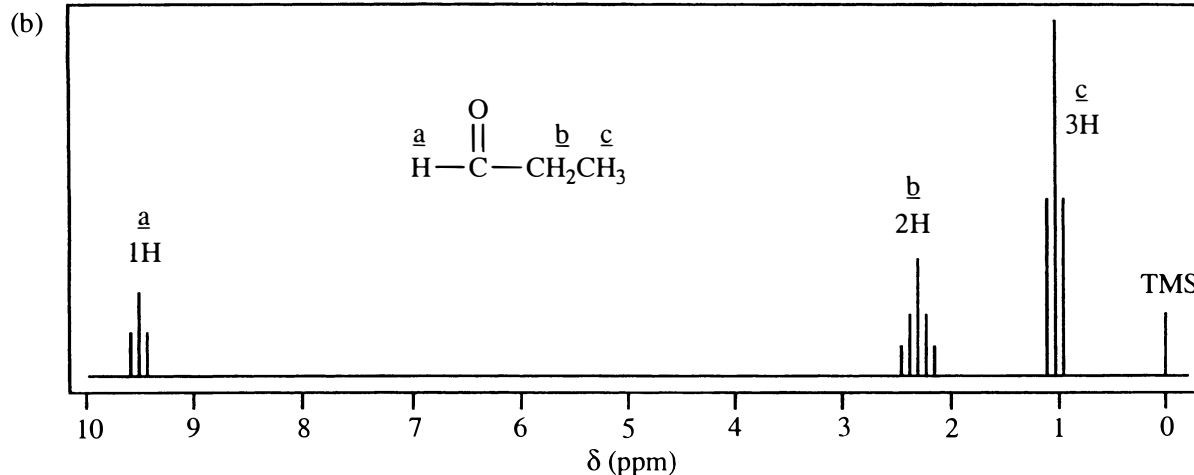
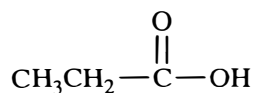


(b) Pentan-1-ol cannot be removed from pentanal by acid-base extraction. These two remaining products can be separated by distillation, the alcohol having the higher boiling point because of hydrogen bonding.

20-7 The COOH has a characteristic IR absorption: a broad peak from $3400\text{--}2400\text{ cm}^{-1}$, with a "shoulder" around 2700 cm^{-1} . The carbonyl stretch at 1695 cm^{-1} is a little lower than the standard 1710 cm^{-1} , suggesting conjugation. The strong alkene absorption at 1650 cm^{-1} also suggests it is conjugated.

20-8

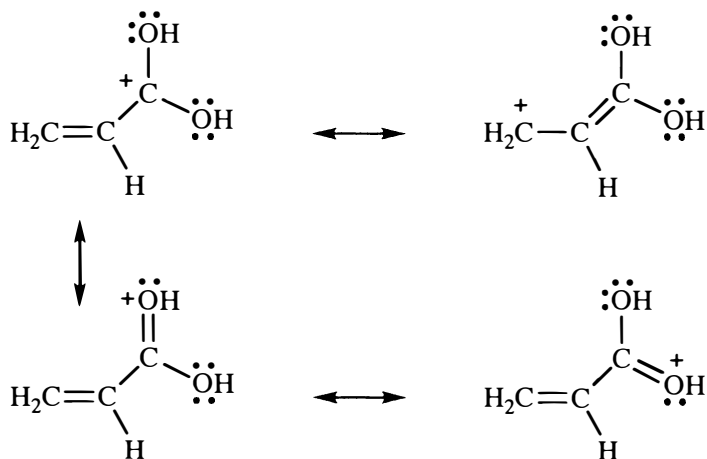
(a) The ethyl pattern is obvious: a 3H triplet at δ 1.15 and a 2H quartet at δ 2.4. The only other peak is the COOH at δ 11.9 (a 2.1 δ unit offset added to 9.8).



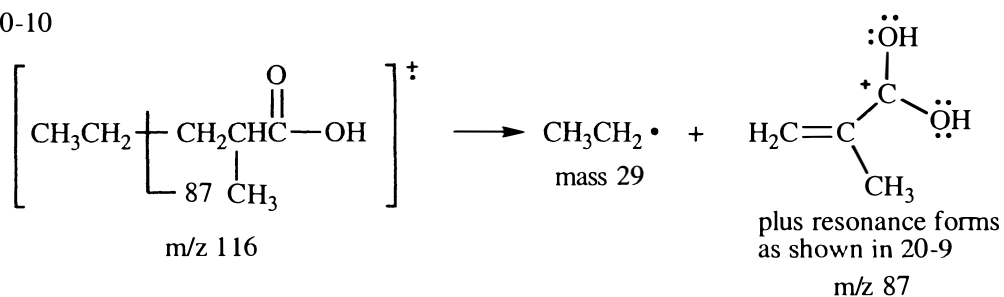
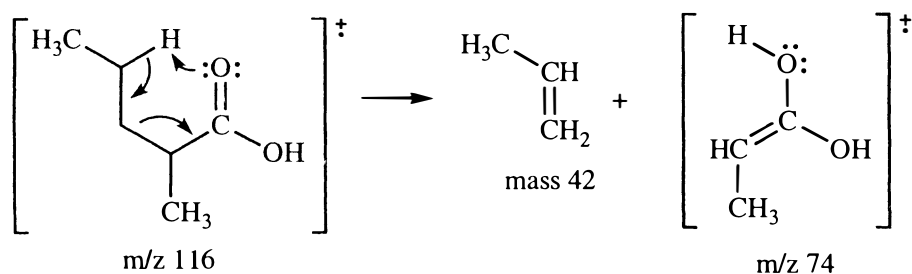
The multiplet between δ 2 and δ 3 is drawn as a pentet as though it were split equally by the aldehyde proton and the CH_2 group. These coupling constants are probably unequal, in which case the actual splitting pattern will be a complex multiplet.

(c) The chemical shift of the aldehyde proton is between δ 9-10, not as far downfield as the carboxylic acid proton. Also, the aldehyde proton is split into a triplet by the CH_2 , unlike the COOH proton which always appears as a singlet. Finally, the CH_2 is split by an extra proton, so it will give a multiplet with complex splitting, instead of the quartet shown in the acid.

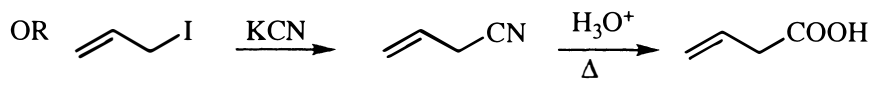
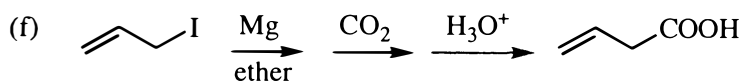
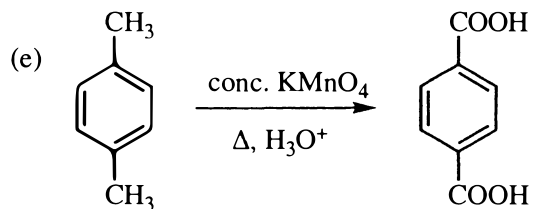
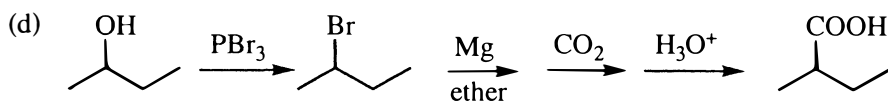
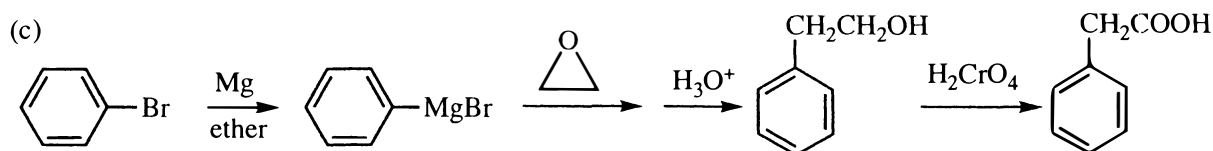
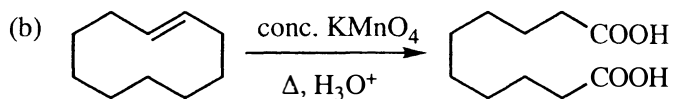
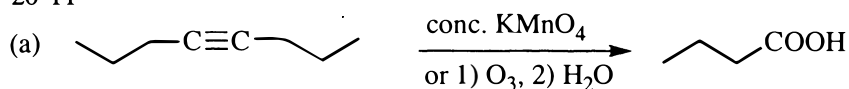
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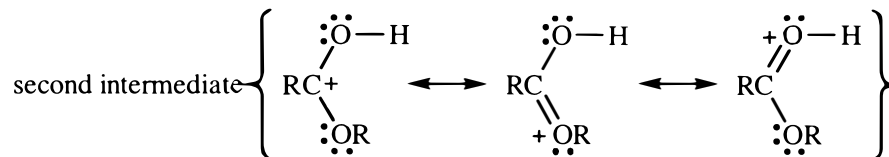
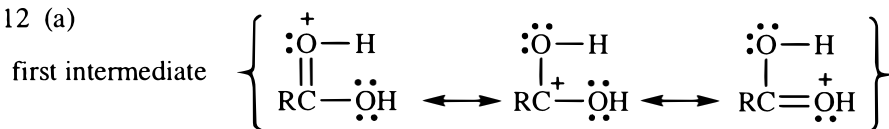
20-10

McLafferty rearrangement

20-11



20-12 (a)



(b) The mechanism of acid-catalyzed nucleophilic acyl substitution may seem daunting, but it is simply a succession of steps that are already very familiar to you.

Typically, these mechanisms have six steps: four proton transfers (two on, two off), a nucleophilic attack, and a leaving group leaving, with a little resonance stabilization thrown in that makes the whole thing work. The six steps are labeled in the mechanism below:

Step A proton on (resonance stabilization)

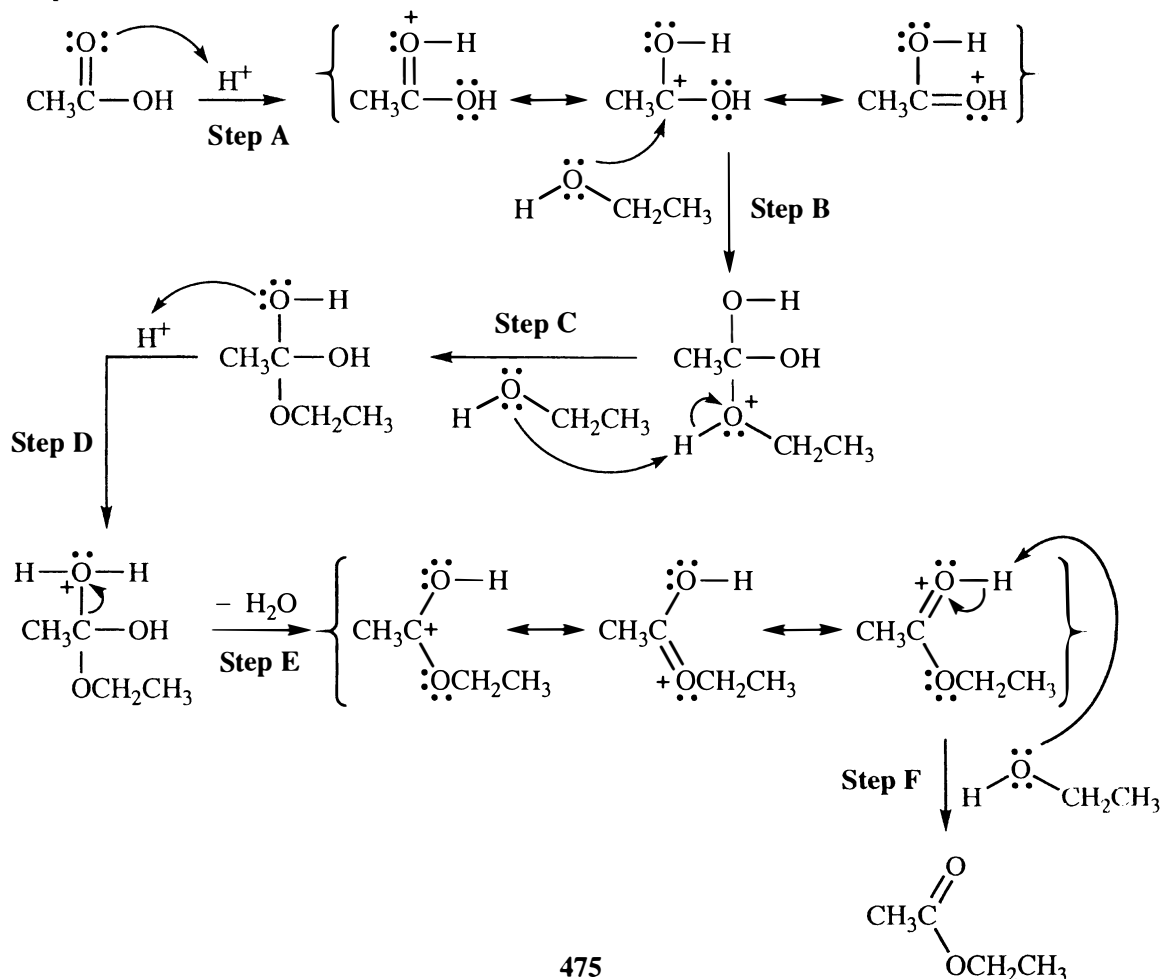
Step B nucleophile attacks

Step C proton off

Step D proton on

Step E leaving group leaves (resonance stabilization)

Step F proton off



20-12 (c) All steps are reversible, which is the reason the Principle of Microscopic Reversibility applies. Applying the steps as outlined on the previous page: (abbreviating OCH_2CH_3 as OEt)

Step A proton on (resonance stabilization)

Step B nucleophile attacks

Step C proton off

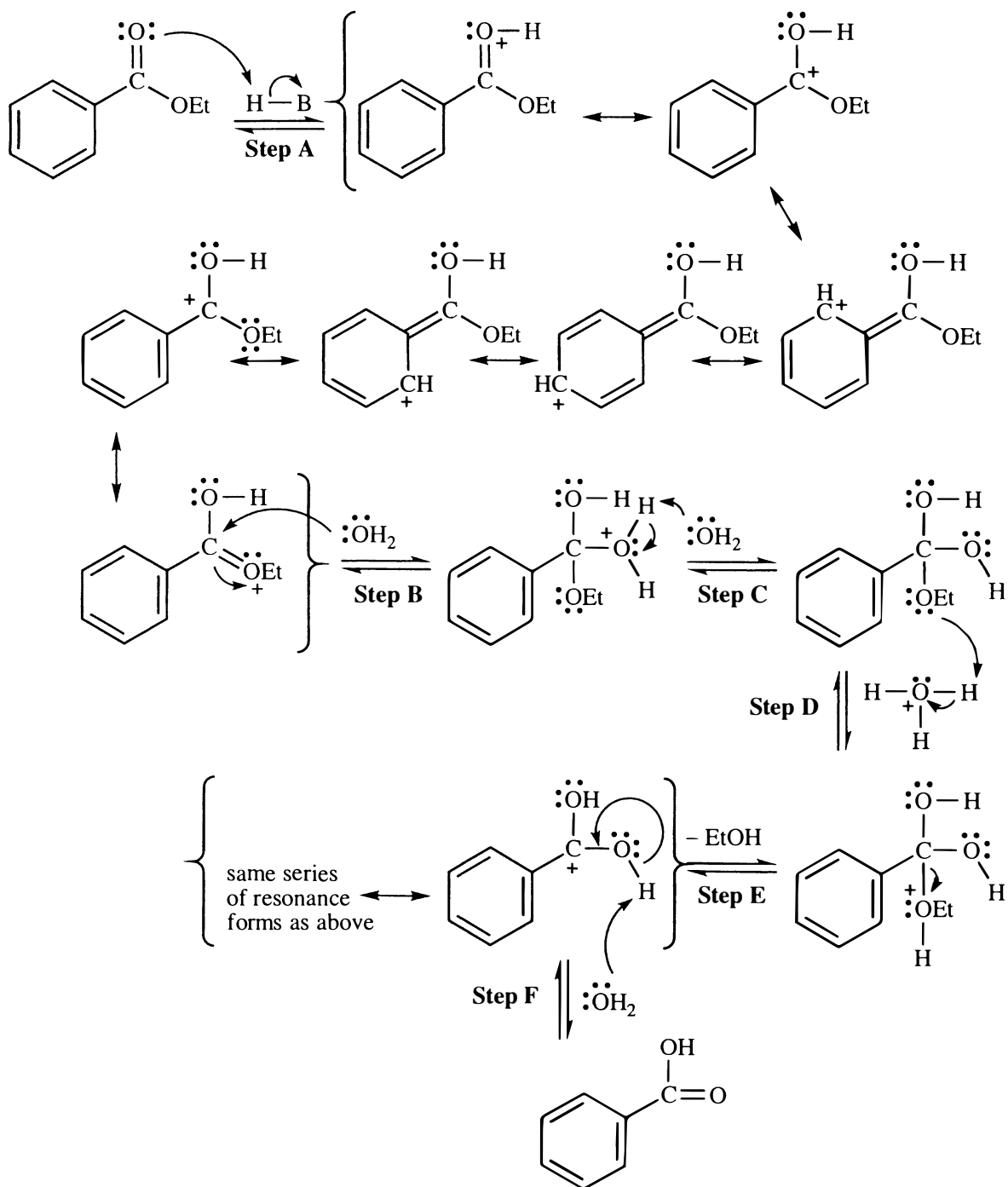
Step D proton on

Step E leaving group leaves (resonance stabilization)

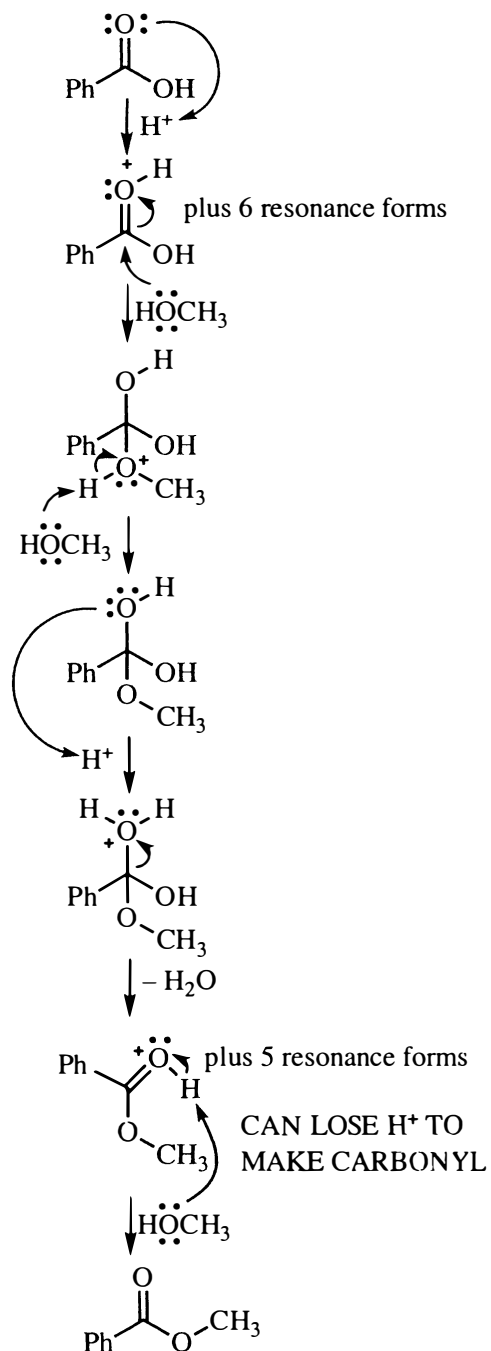
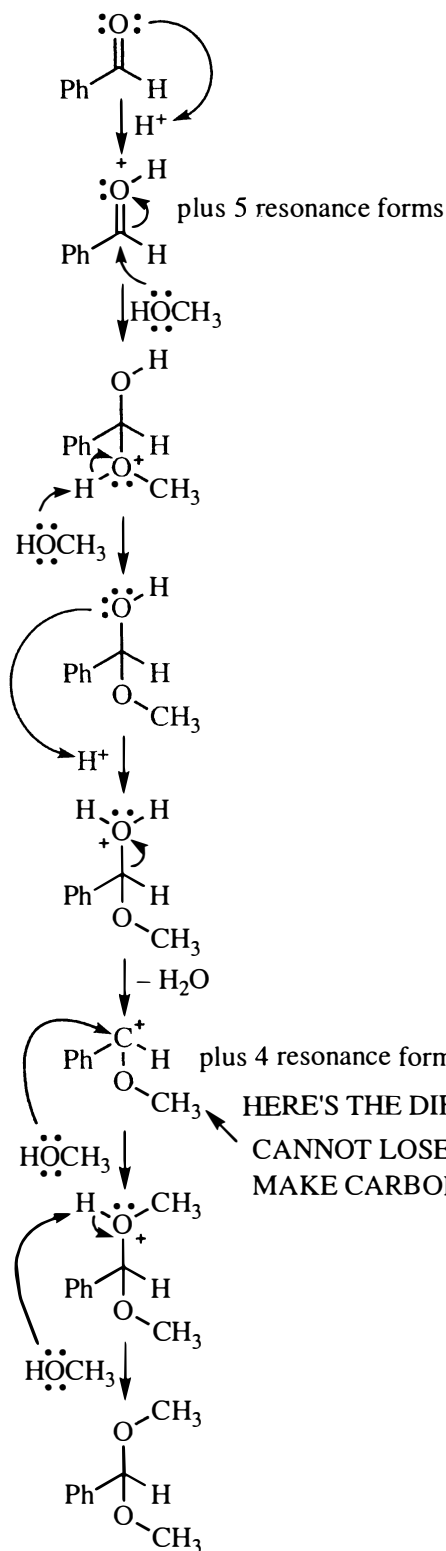
Step F proton off

$\text{H}-\text{B}$ is the acid catalyst

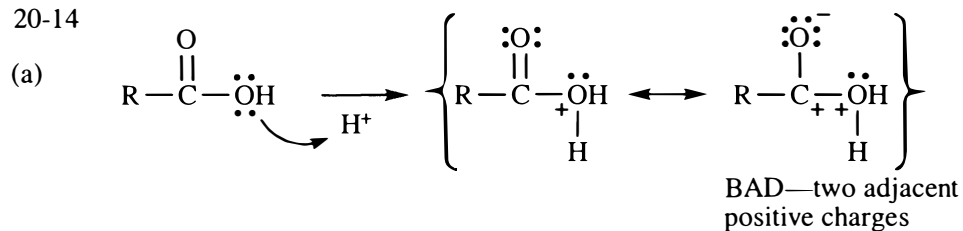
$:\text{B}^-$ is the conjugate base, although in hydrolysis reactions, water usually removes H^+



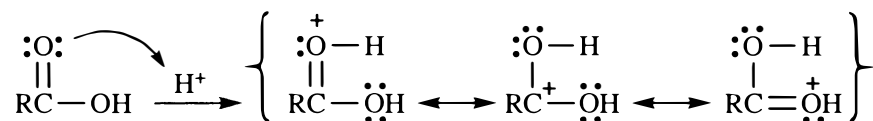
20-13 For the sake of space in this problem, resonance forms will not be drawn, but remember that they are critical!



20-14

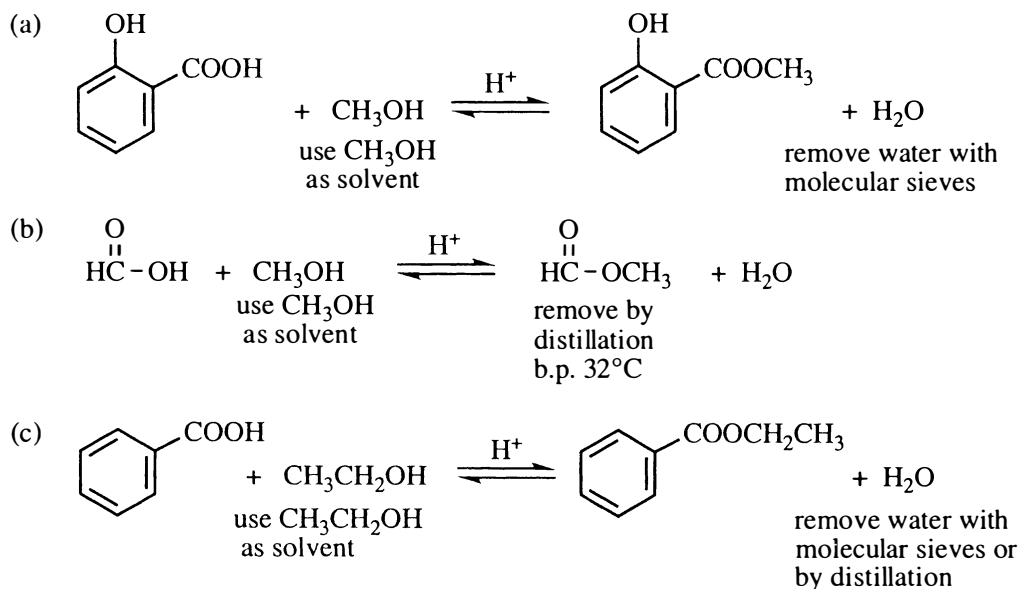


(b) Protonation on the OH gives only two resonance forms, one of which is bad because of adjacent positive charges. Protonation on the C=O is good because of three resonance forms distributing the positive charge over three atoms, with no additional charge separation.



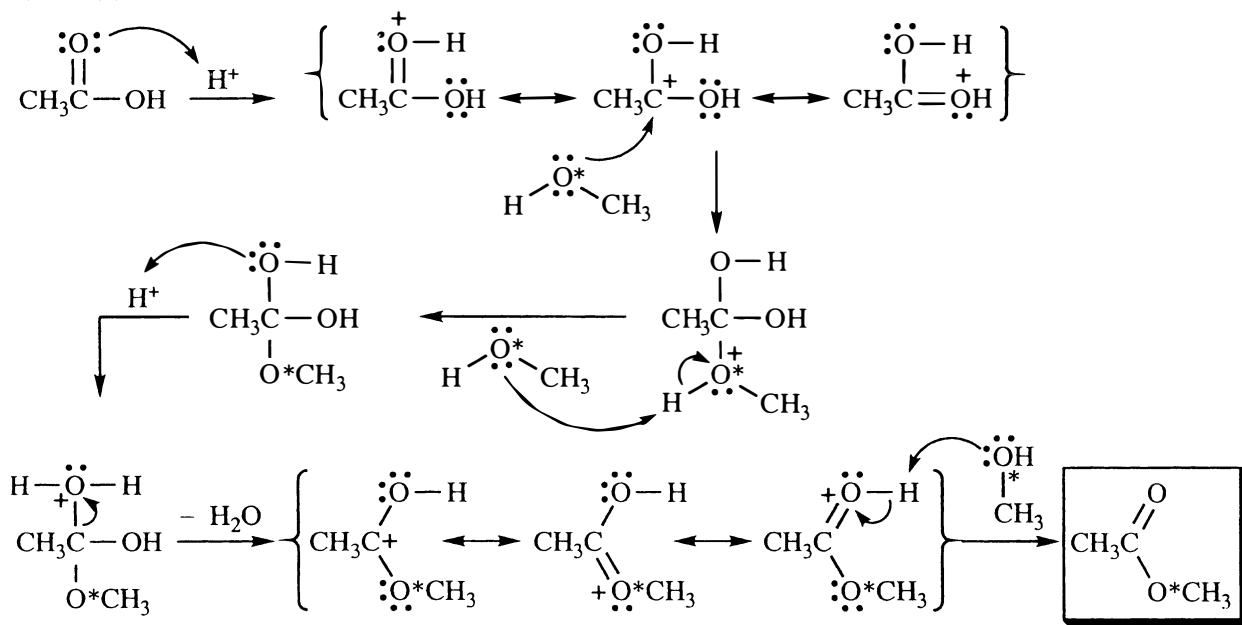
(c) The carbonyl oxygen is more "basic" because, by definition, it reacts with a proton more readily. It does so because the intermediate it produces is more stable than the intermediate from protonation of the OH.

20-15



20-16 The asterisk ("*") denotes the ^{18}O isotope.

(a) and (b)

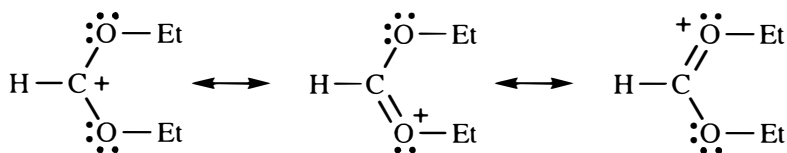


(c) The ^{18}O has two more neutrons, and therefore two more mass units, than ^{16}O . The instrument ideally suited to analyze compounds of different mass is the mass spectrometer.

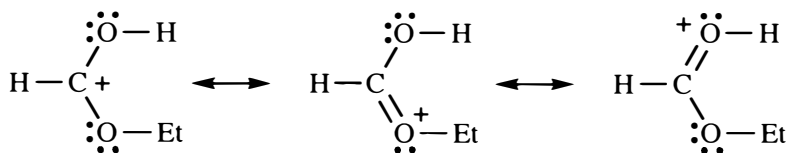
20-17

(a)

first intermediate:

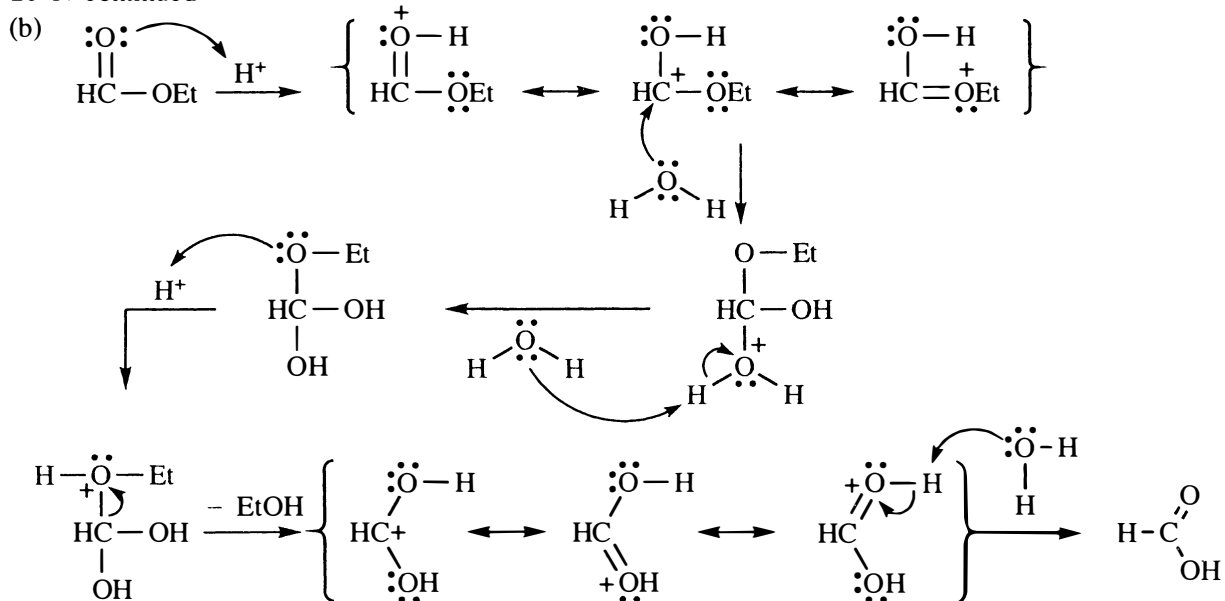


second intermediate:

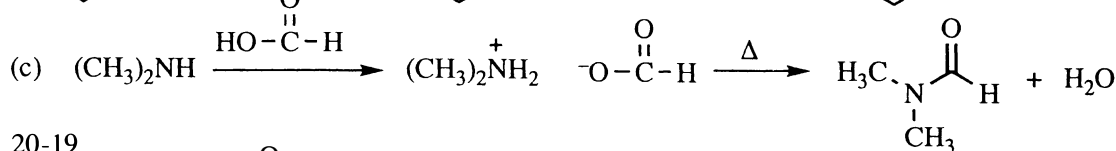
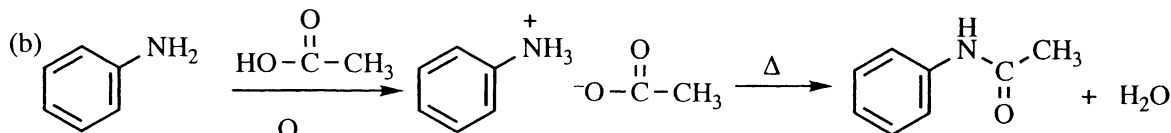
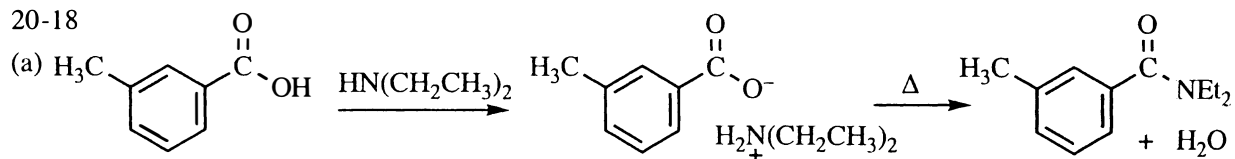


The more resonance forms that can be drawn to represent an intermediate, the more stable the intermediate. The more stable the intermediate, the more easily it can be formed, that is, under milder conditions. These intermediates are highly stabilized due to delocalization of the positive charge over the carbon and both oxygens. A trace of acid is all that is required to initiate this process.

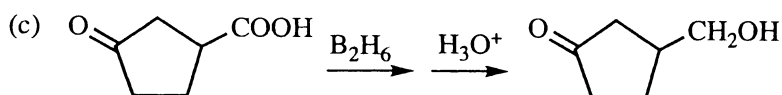
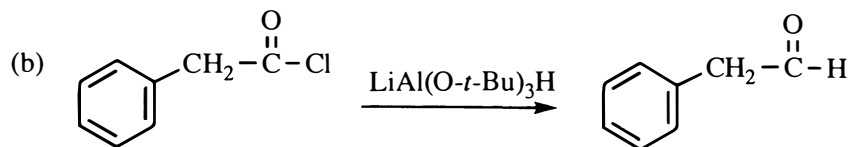
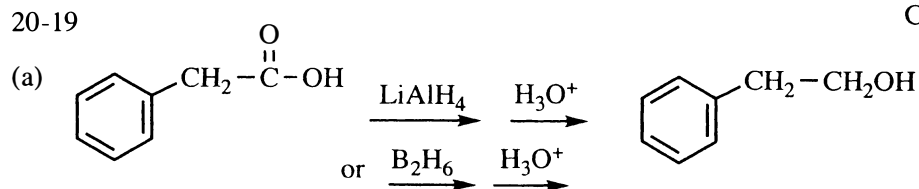
20-17 continued



20-18

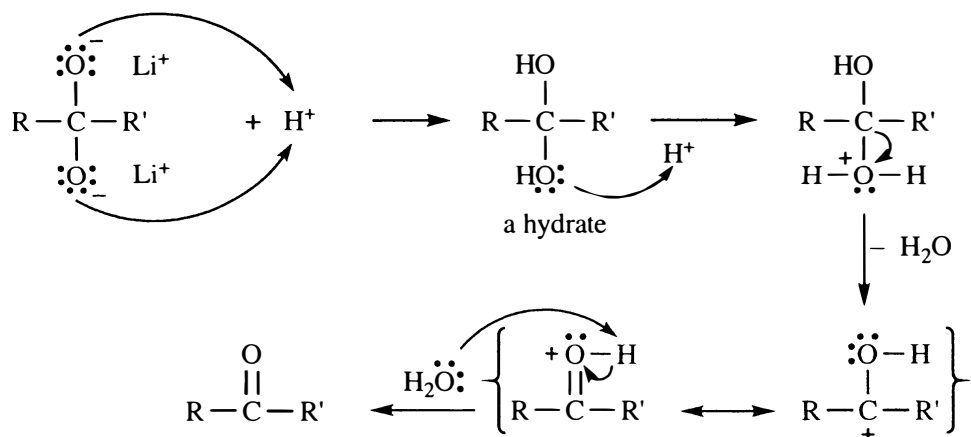


20-19

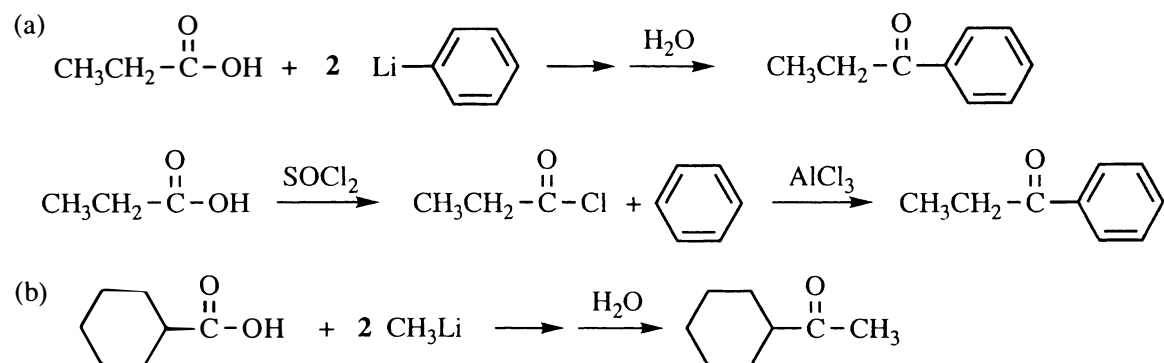


B_2H_6 selectively reduces a carboxylic acid in the presence of a ketone. Alternatively, protecting the ketone as an acetal, reducing the COOH , and removing the protecting group would also be possible but longer.

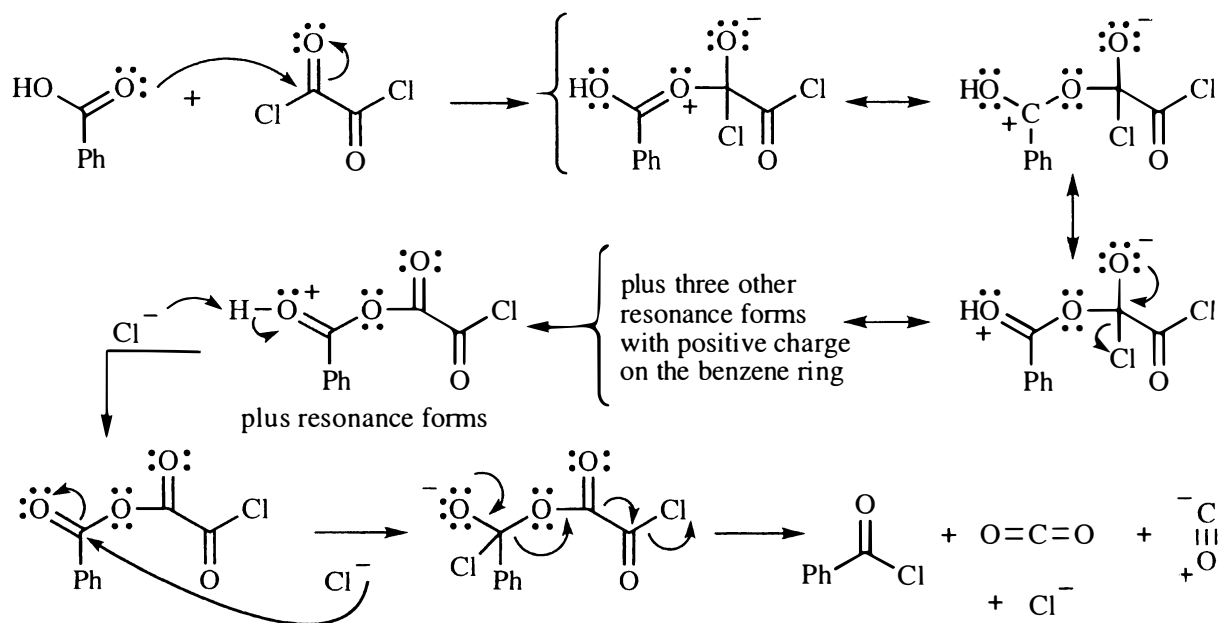
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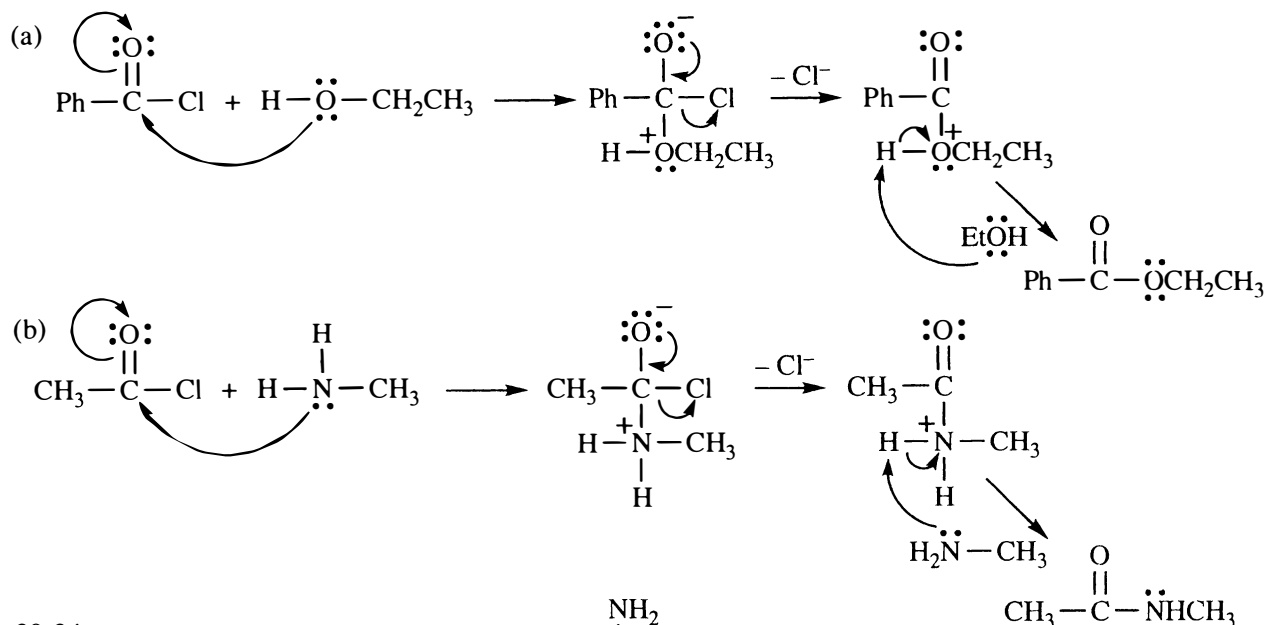
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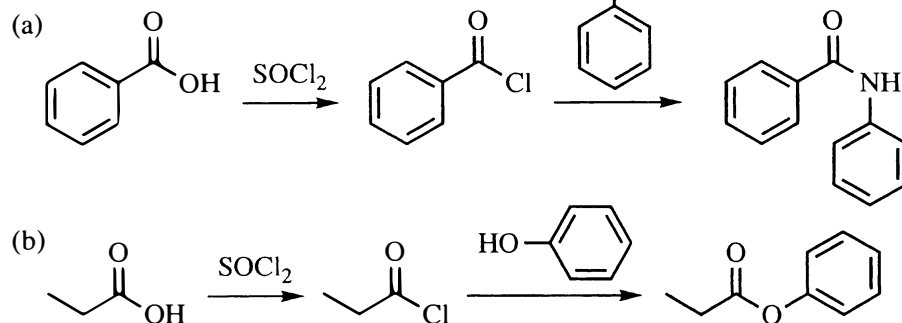
20-22



20-23



20-24



20-25 Please refer to solution 1-20, page 12 of this Solution Manual.

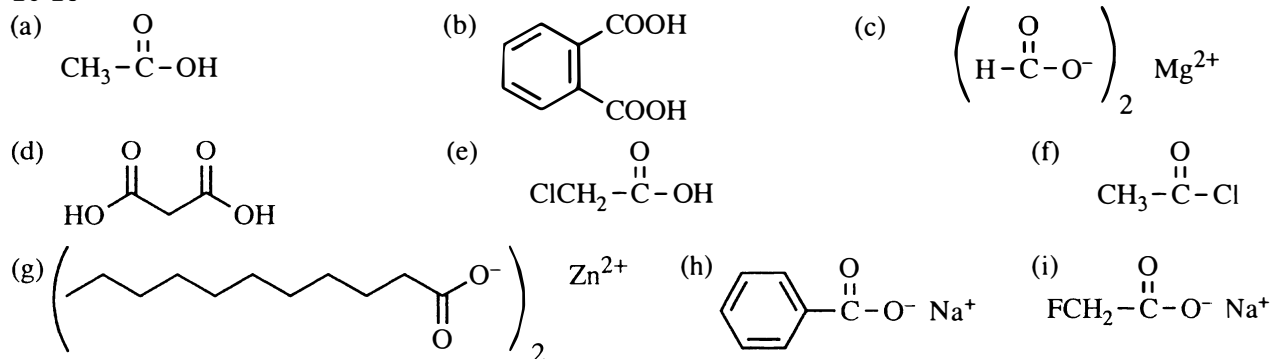
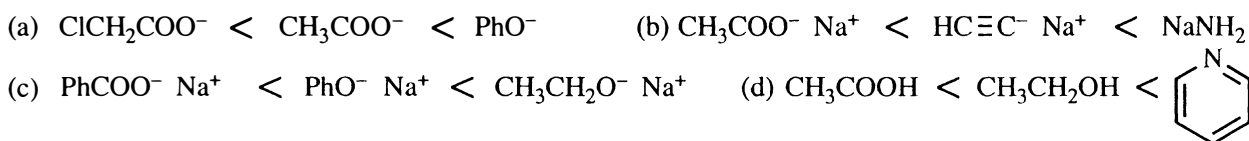
20-26

- | | |
|---|--------------------------------|
| (a) 3-phenylpropanoic acid | (b) 2-methylbutanoic acid |
| (c) 2-bromo-3-methylbutanoic acid | (d) 2-methylbutanedioic acid |
| (e) sodium 2-methylbutanoate | (f) 3-methylbut-2-enoic acid |
| (g) <i>trans</i> -2-methylcyclopentanecarboxylic acid | (h) 2,4,6-trinitrobenzoic acid |
| (i) 7,7-dimethyl-4-oxooctanoic acid | |

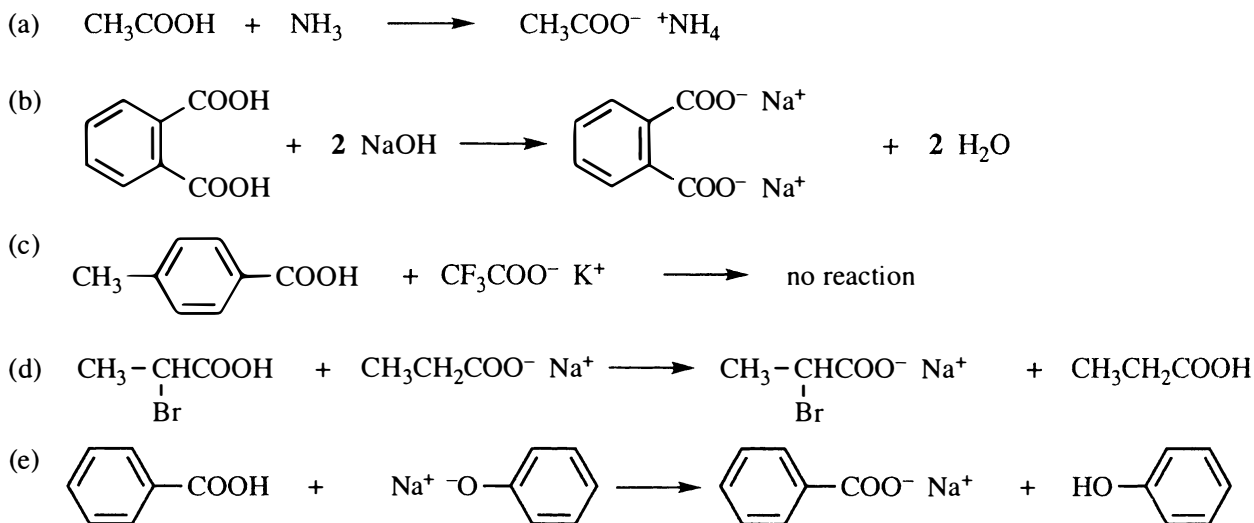
20-27

- | | |
|--|-----------------------------------|
| (a) β -phenylpropionic acid | (b) α -methylbutyric acid |
| (c) α -bromo- β -methylbutyric acid,
or α -bromoisovaleric acid | (d) α -methylsuccinic acid |
| (e) sodium β -methylbutyrate | (f) β -aminobutyric acid |
| (g) <i>o</i> -bromobenzoic acid | (h) magnesium oxalate |
| (i) 4-methoxyphthalic acid | |

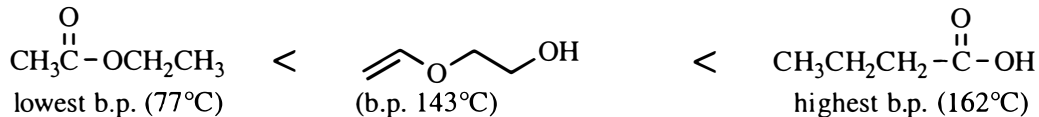
20-28

20-29 Weaker base listed first. (Weaker bases come from *stronger* conjugate acids.)

20-30



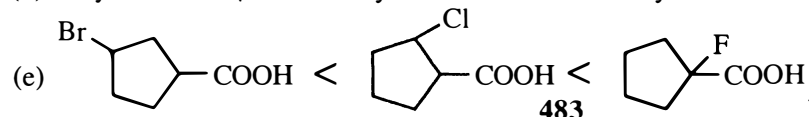
20-31



The ester cannot form hydrogen bonds and will be the lowest boiling. The alcohol can form hydrogen bonds. The carboxylic acid forms two hydrogen bonds and boils as the dimer, the highest boiling among these three compounds.

20-32 Listed in order of increasing acidity (weakest acid first):

- (a) ethanol < phenol < acetic acid
 (b) acetic acid < chloroacetic acid < *p*-toluenesulfonic acid
 (c) benzoic acid < *m*-nitrobenzoic acid < *o*-nitrobenzoic acid
 (d) butyric acid < β -bromobutyric acid < α -bromobutyric acid



EWG = electron-withdrawing group

- Acidity increases with:
1. closer proximity of EWG
 2. great number of EWG
 3. increasing strength (electronegativity) of EWG

20-33 Acetic acid derivatives are often used as a test of electronic effects of a series of substituents: they are fairly easily synthesized (or are commercially available), and pK_a values are easily measured by titration.

Substituents on carbon-2 of acetic acid can express only an inductive effect; no resonance effect is possible because the CH_2 is sp^3 hybridized and no π overlap is possible.

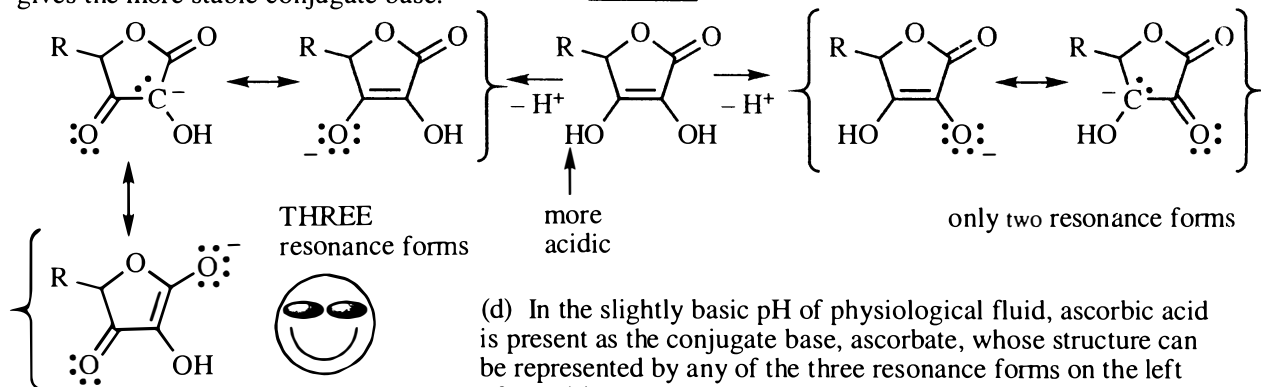
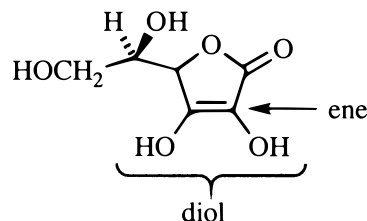
Two conclusions can be drawn from the given pK_a values. First, all four substituents are electron-withdrawing because all four substituted acids are stronger than acetic acid. Second, the magnitude of the electron-withdrawing effect increases in the order: $OH < Cl < CN < NO_2$. (It is always a safe assumption that nitro is the strongest electron-withdrawing group of all the common substituents.)

20-34

(a) Ascorbic acid is not a carboxylic acid. It is an example of a structure called an ene-diol where one of the OH groups is unusually acidic because of the adjacent carbonyl group. See part (c).

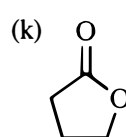
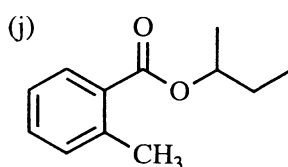
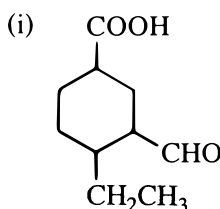
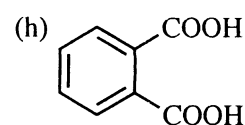
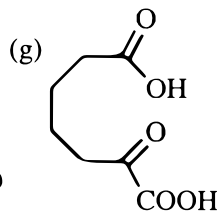
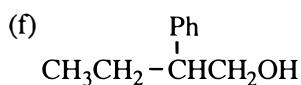
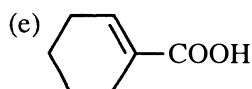
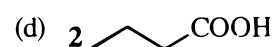
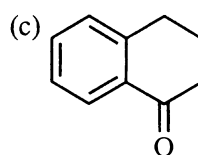
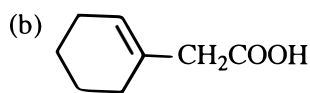
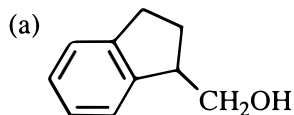
(b) Ascorbic acid, pK_a 4.71, is almost identical to the acidity of acetic acid, pK_a 4.74.

(c) The more acidic H will be the one that, when removed, gives the more stable conjugate base. *start here*

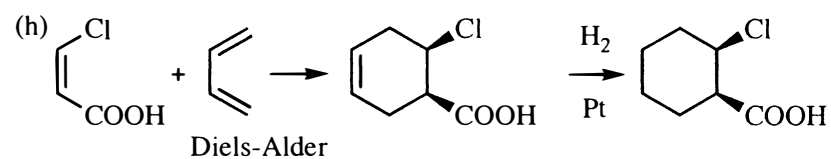
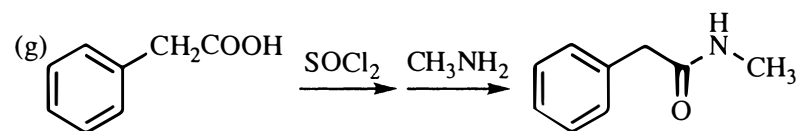
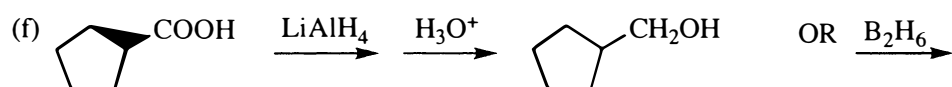
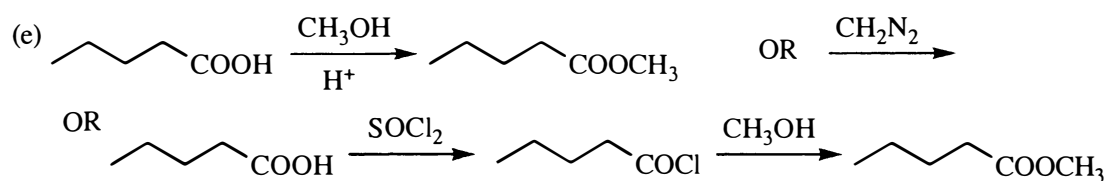
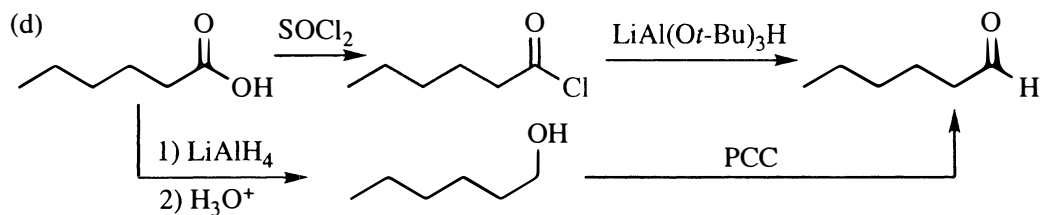
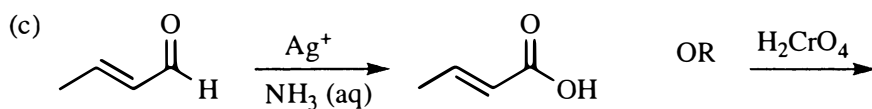
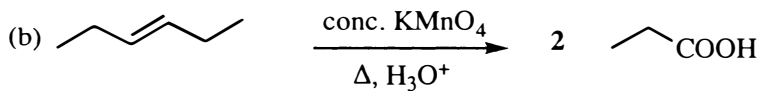
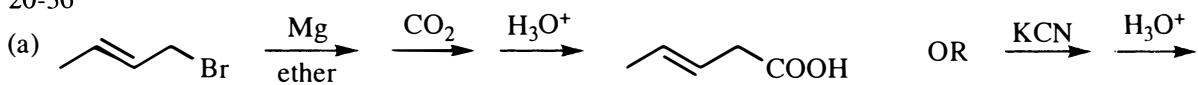


(d) In the slightly basic pH of physiological fluid, ascorbic acid is present as the conjugate base, ascorbate, whose structure can be represented by any of the three resonance forms on the left of part (c).

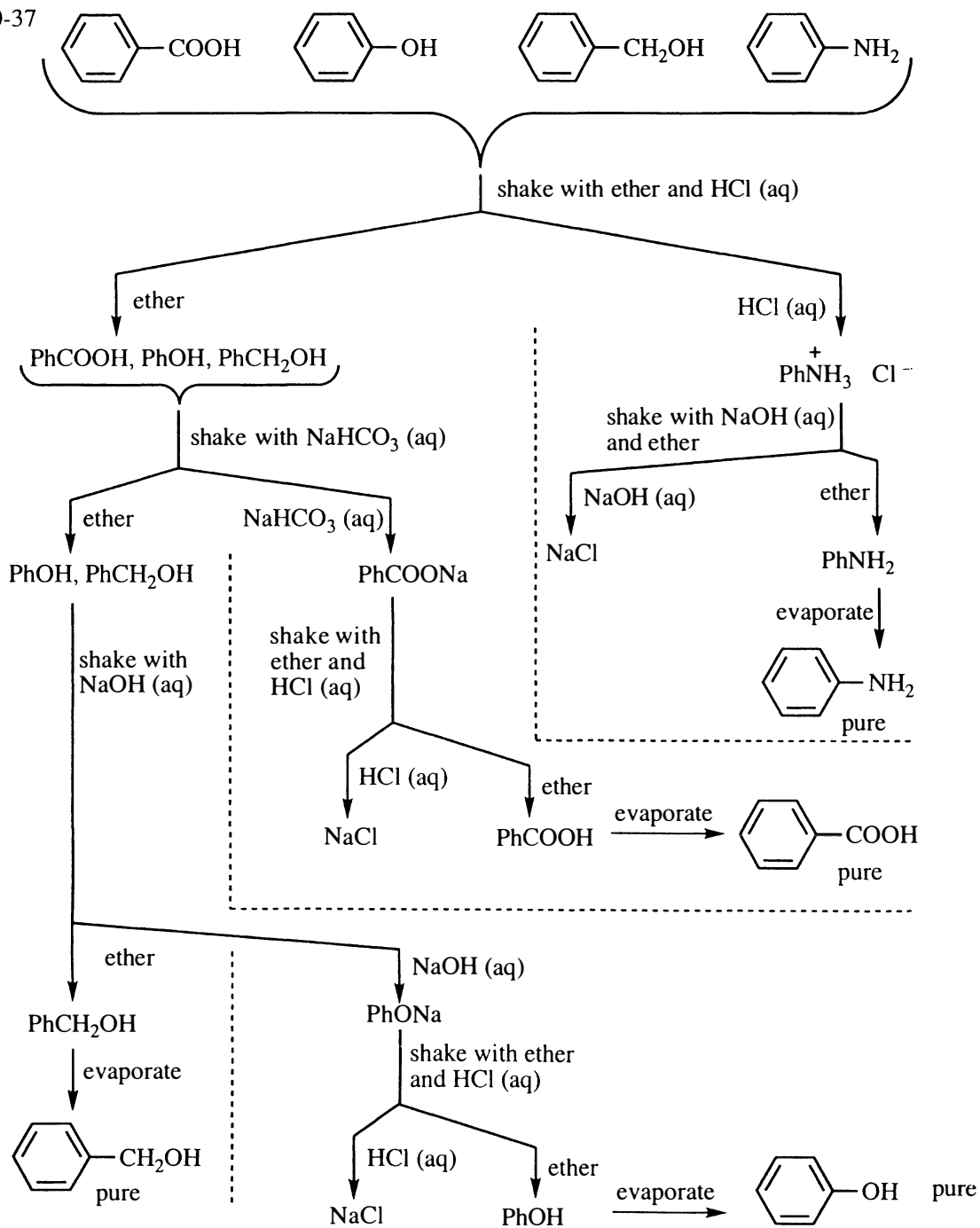
20-35



20-36

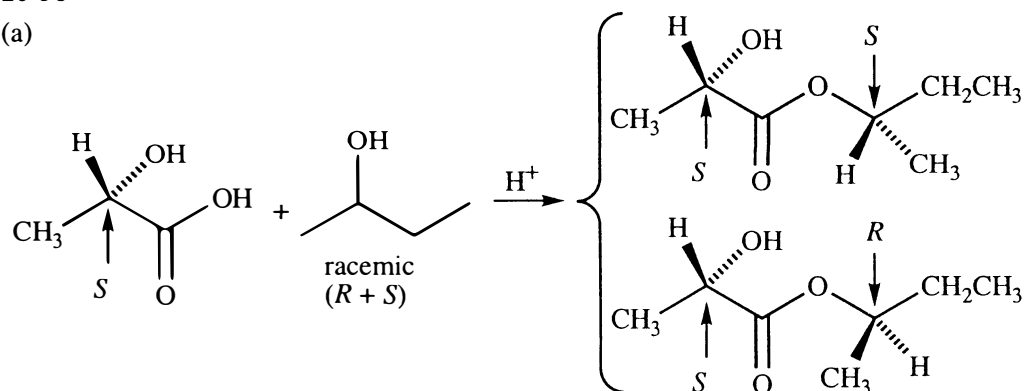


20-37

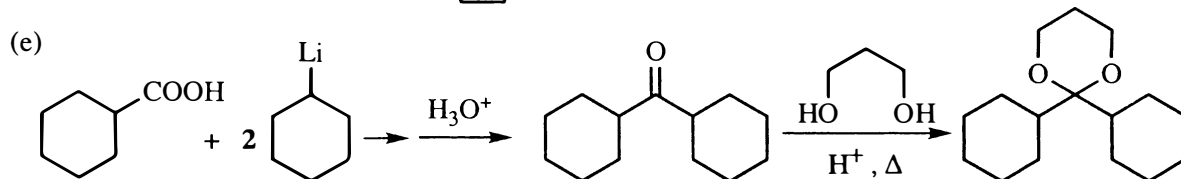
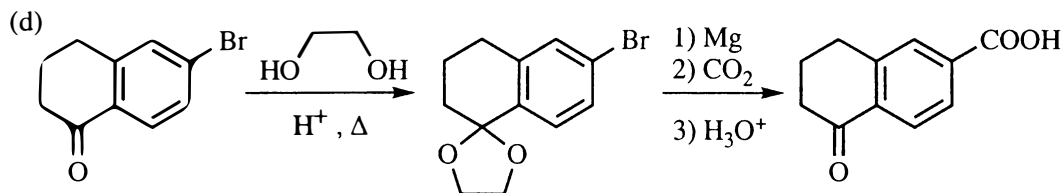
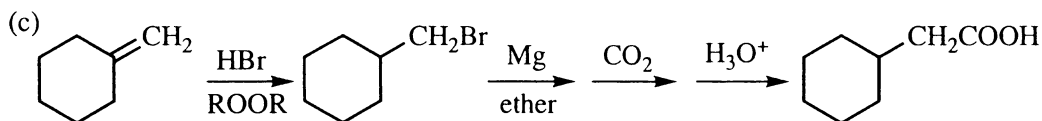
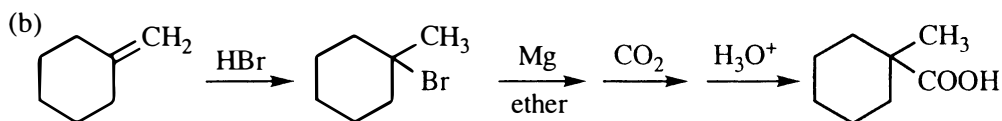
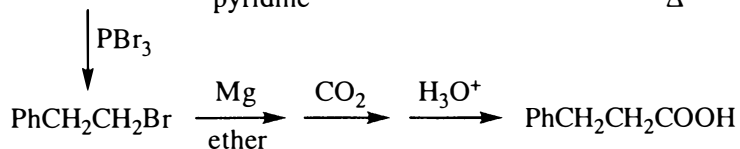
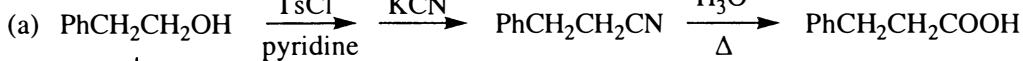


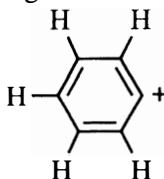
20-38

(a)

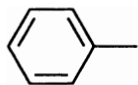
(b) Isomers which are *R,S* and *S,S* are diastereomers.

20-39

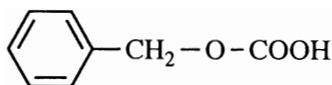
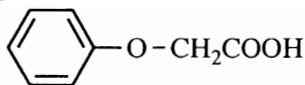


(a) Mass spectrum:— m/z 152 $\Rightarrow$ molecular ion $\Rightarrow$ molecular weight 152— m/z 107 $\Rightarrow M - 45 \Rightarrow$ loss of COOH— m/z 77 $\Rightarrow$ monosubstituted benzene ring,IR spectrum:— $3400\text{--}2400\text{ cm}^{-1}$, broad $\Rightarrow$ O—H stretch of COOH— $1700\text{ cm}^{-1} \Rightarrow$ C=O— $1240\text{ cm}^{-1} \Rightarrow$ C—O— $1600\text{ cm}^{-1} \Rightarrow$ aromatic C=CNMR spectrum:— δ 6.8–7.3, two signals in the ratio of 2H to 3H $\Rightarrow$ monosubstituted benzene ring— δ 4.6, 2H singlet $\Rightarrow$ CH₂, deshieldedCarbon NMR spectrum:— δ 170, small peak $\Rightarrow$ carbonyl— δ 115–157, four peaks $\Rightarrow$ monosubstituted benzene ring; deshielded peak indicates oxygen substitution on the ring

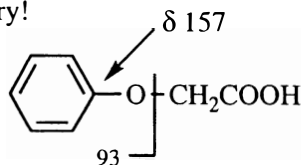
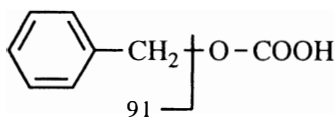
(b) Fragments indicated in the spectra:

 m/z 77CH₂
 m/z 14COOH
 m/z 45 and from IR

This appears deceptively simple. The problem is that the mass of these fragments adds to 136, not 152—we are missing 16 mass units $\Rightarrow$ oxygen! Where can the oxygen be? There are only two possibilities:



How can we differentiate? Mass spectrometry!



phenoxyacetic acid

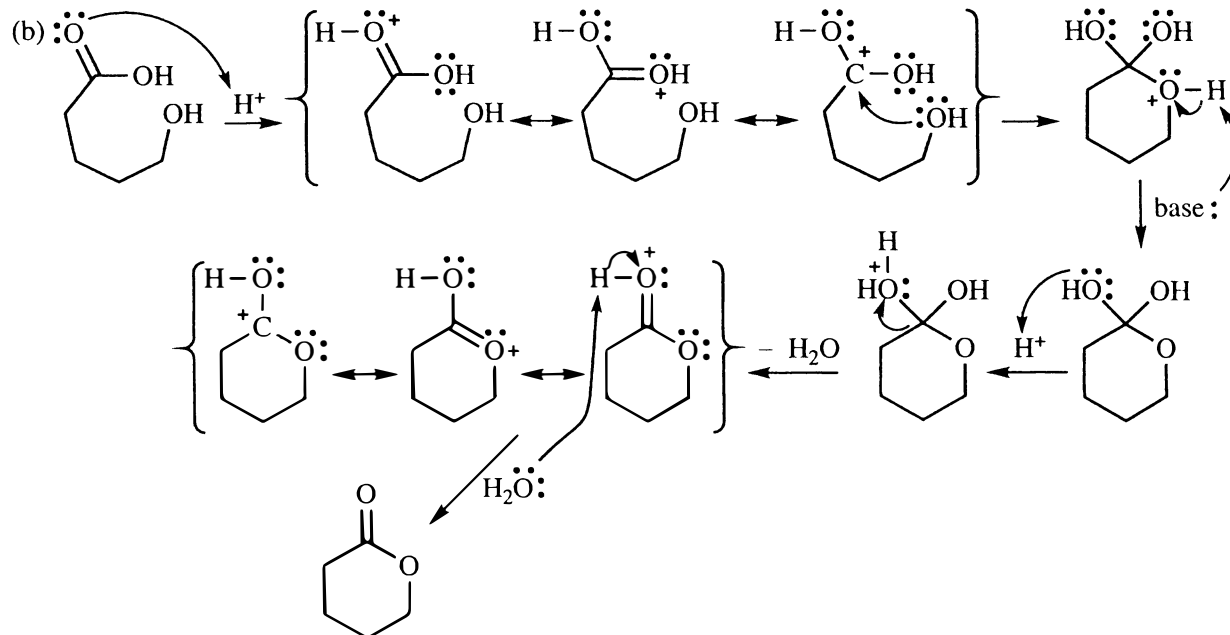
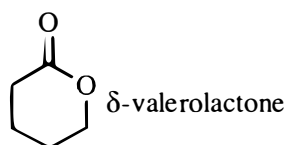
This structure is consistent with the peak at δ 157 in the carbon NMR.

The m/z 93 peak in the MS confirms the structure is **phenoxyacetic acid**. The CH₂ is so far downfield in the NMR because it is between two electron-withdrawing groups, the O and the COOH.

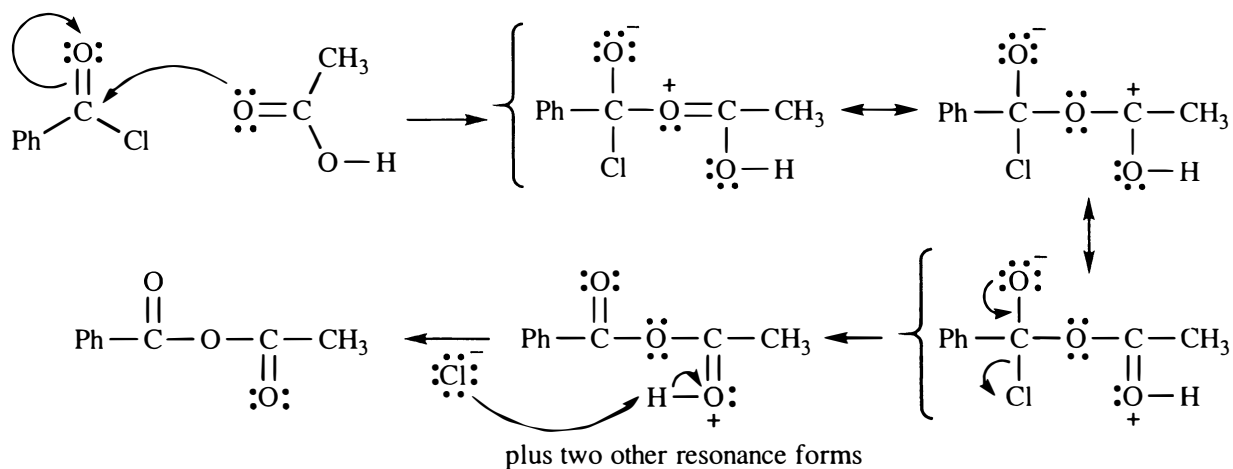
(c) The COOH proton is missing from the proton NMR. Either it is beyond 10 and the NMR was not scanned (unlikely), or the peak was broadened beyond detection because of hydrogen bonding with DMSO.

20-41

(a)

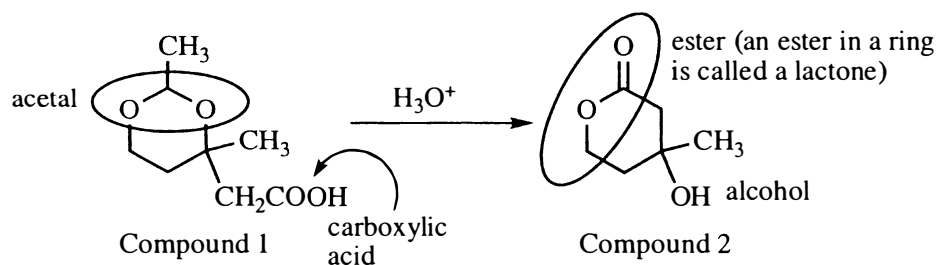


20-42



20-43

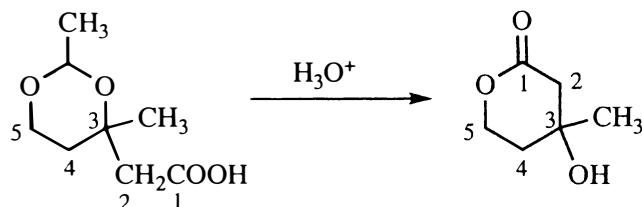
(a)



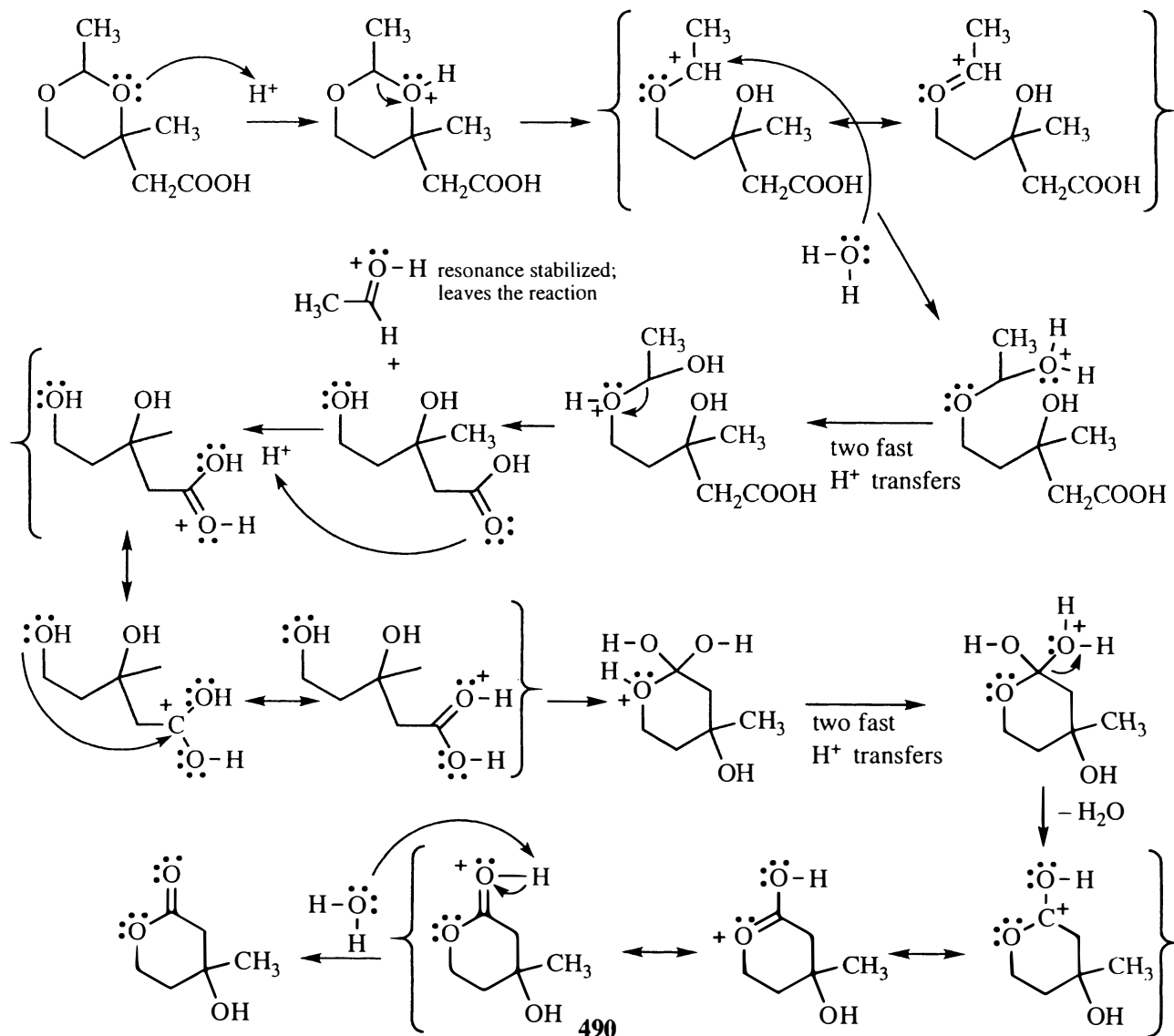
20-43 continued

(b) Compound 1 has 8 carbons, and Compound 2 has 6 carbons. Two carbons have been lost: the two carbons of the acetal have been cleaved. (This is the best way to figure out reactions and mechanisms: find out which atoms of the reactant have become which atoms of the product, then determine what bonds have been broken and formed.)

(c) Acetals are stable to base, so the acetal must have been cleaved when acid was added.



(d) The carbons have been numbered above to help you visualize which atoms in the reactant become which atoms in the product. The overall process requires cleavage of the acetal to expose two alcohols. The 3° alcohol at carbon-3 can be found in the product, so it is the primary alcohol at carbon-5 that reacts with the carboxylic acid to form the lactone.



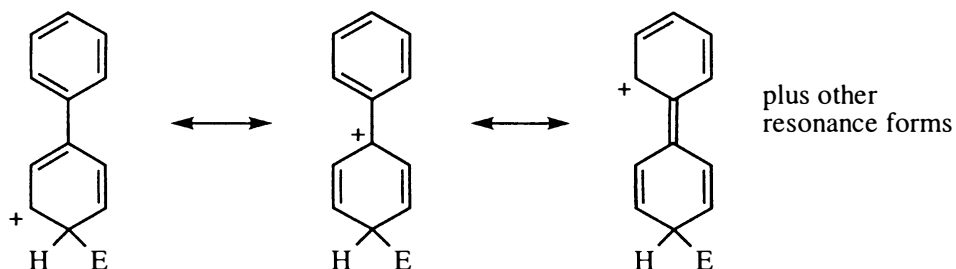
20-44 (A more complete discussion of acidity and electronic effects can be found in Appendix 2.) A few words about the two types of electronic effects: induction and resonance. Inductive effects are a result of polarized σ bonds, usually because of electronegative atom substituents. Resonance effects work through π systems, requiring overlap of p orbitals to delocalize electrons.

All substituents have an inductive effect compared to hydrogen (the reference). Many groups also have a resonance effect; all that is required to have a resonance effect is that the atom or group have at least one p orbital for overlap.

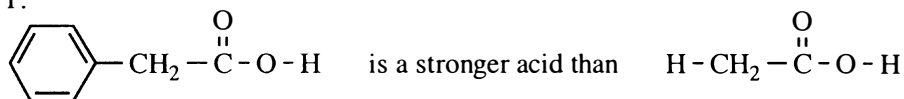
The most interesting groups have both inductive and resonance effects. In such groups, how can we tell the direction of electron movement, that is, whether a group is electron-donating or electron-withdrawing? And do the resonance and inductive effects reinforce or conflict with each other? We can never "turn off" an inductive effect from a resonance effect; that is, any time a substituent is expressing its resonance effect, it is also expressing its inductive effect. We can minimize a group's inductive effect by moving it farther away; inductive effects decrease with distance. The other side of the coin is more accessible to the experimenter: we can "turn off" a resonance effect in order to isolate an inductive effect. We can do this by interrupting a conjugated π system by inserting an sp^3 -hybridized atom, or by making resonance overlap impossible for steric reasons (steric inhibition of resonance).

These three problems are examples of separating inductive effects from resonance effects.

(a) and (b) In electrophilic aromatic substitution, the phenyl substituent is an ortho,para-director because it can stabilize the intermediate from electrophilic attack at the ortho and para positions. The phenyl substituent is electron-donating *by resonance*.



BUT:

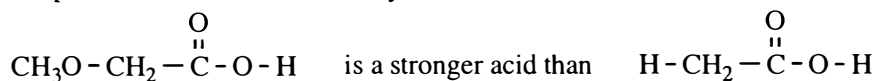


The greater acidity of phenylacetic acid shows that the phenyl substituent is electron-withdrawing, thereby stabilizing the product carboxylate's negative charge. Does this contradict what was said above? Yes and no. What is different is that, since there is no p-orbital overlap between the phenyl group and the carboxyl group because of the CH_2 group in between, the increased acidity must be from a pure *inductive effect*. This structure isolates the inductive effect (which can't be "turned off") from the resonance effect of the phenyl group.

We can conclude three things: (1) phenyl is electron-withdrawing by induction; (2) phenyl is (in this case) electron-donating by resonance; (3) for phenyl, the resonance effect is stronger than the inductive effect (since it is an ortho,para-director).

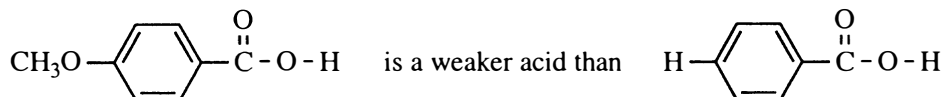
20-44 continued

(c) The simpler case first—induction only:

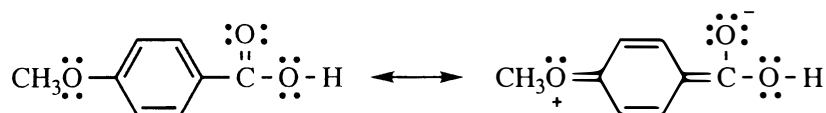


There is no resonance overlap between the methoxy group and the carboxyl group, so this is a pure inductive effect. The methoxy substituent increases the acidity, so methoxy must be electron-withdrawing by induction. This should come as no surprise as oxygen is the second most electronegative element.

The anomaly comes in the decreased acidity of 4-methoxybenzoic acid:

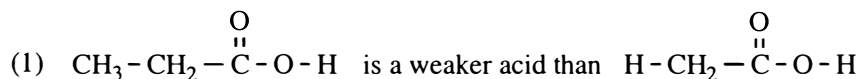


Through resonance, a pair of electrons from the methoxy oxygen can be donated through the benzene ring to the carboxyl group—a stabilizing effect. However, this electron donation *destabilizes* the carboxylate anion as there is already a negative charge on the carboxyl group; the resonance donation intensifies the negative charge. Since the product of the equilibrium would be destabilized relative to the starting material, the proton donation would be less favorable, which we define as a weaker acid.

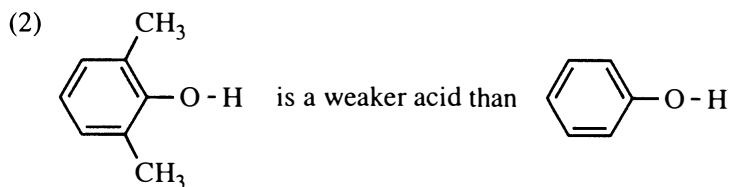


Methoxy is another example of a group which is electron-withdrawing by induction but electron-donating by resonance.

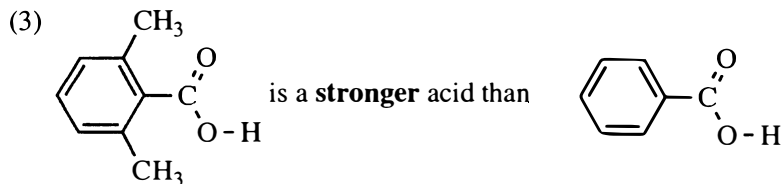
(d) This problem gives three pieces of data to interpret:



Interpretation: the methyl group is electron-donating by induction.



Interpretation: the methyl group is electron-donating by induction. This interpretation is consistent with (1), as expected, since methyl cannot have any resonance effect.

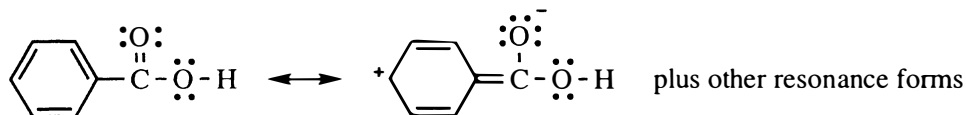


Interpretation: this is the anomaly. Contradictory to the data in (1) and (2), by putting on two methyl groups, the substituent seems to have become electron-withdrawing instead of electron-donating. How?

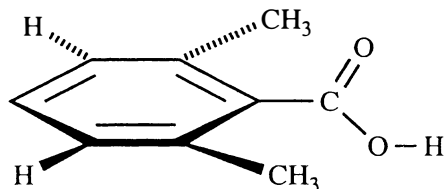
Quick! Turn the page!

20-44 continued

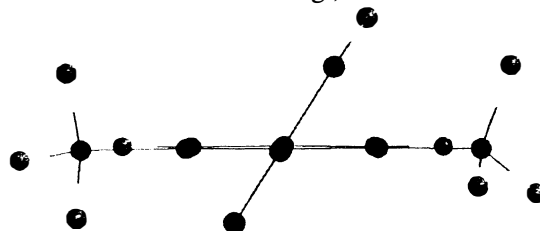
Steric inhibition of resonance! In benzoic acid, the phenyl ring and the carboxyl group are all in the same plane, and benzene is able to donate electrons by resonance overlap through parallel p orbitals. This stabilizes the starting acid (and destabilizes the carboxylate anion) and makes the acid weaker than it would be without resonance.



Putting substituents at the 2- and 6-positions prevents the carboxyl or carboxylate from coplanarity with the ring. Resonance is interrupted, and now the carboxyl group sees a phenyl substituent which cannot stabilize the acid through resonance; the stabilization of the acid is lost. At the same time, the *electron-withdrawing inductive effect* of the benzene ring stabilizes the carboxylate anion. These two effects work together to make this acid unusually strong. (Apparently, the slight electron-donating inductive effect of the methyls is overpowered by the stronger electron-withdrawing inductive effect of the benzene ring.)



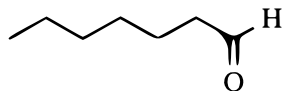
COOH group is perpendicular to the plane of the benzene ring—no resonance interaction.



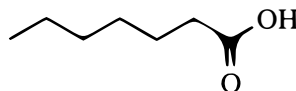
this three-dimensional view down the C-C bond between the COOH and the benzene ring shows that COOH is twisted out of the benzene plane

20-45

(a)



stock bottle

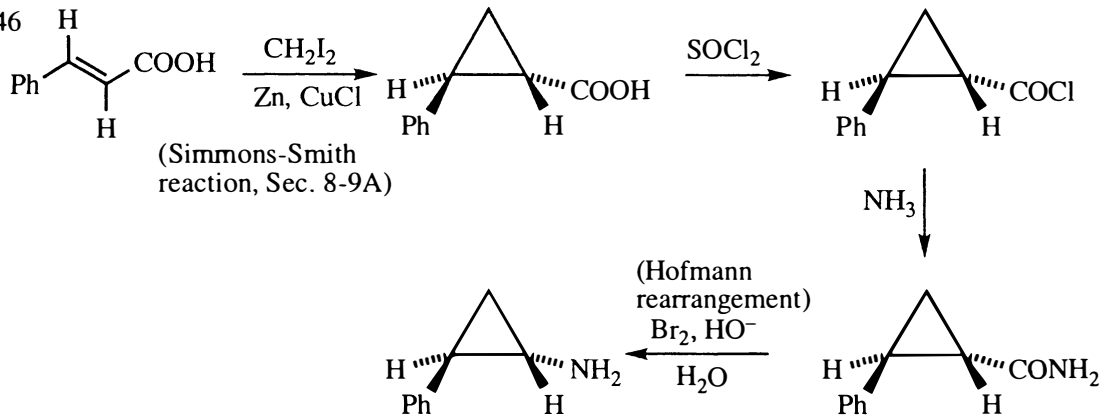


students' samples

(b) The spectrum of the students' samples shows the carboxylic acid present. Contact with oxygen from the air oxidized the sensitive aldehyde group to the acid.

(c) Storing the aldehyde in an inert atmosphere like nitrogen or argon prevents oxidation. Freshly prepared unknowns will avoid the problem.

20-46



20-47 Products are boxed.

(a) All steps are reversible in an acid-catalyzed ester hydrolysis. (abbreviating OCH_2CH_3 as OEt)

Step A proton on (resonance stabilization)

Step B nucleophile attacks

Step C proton off

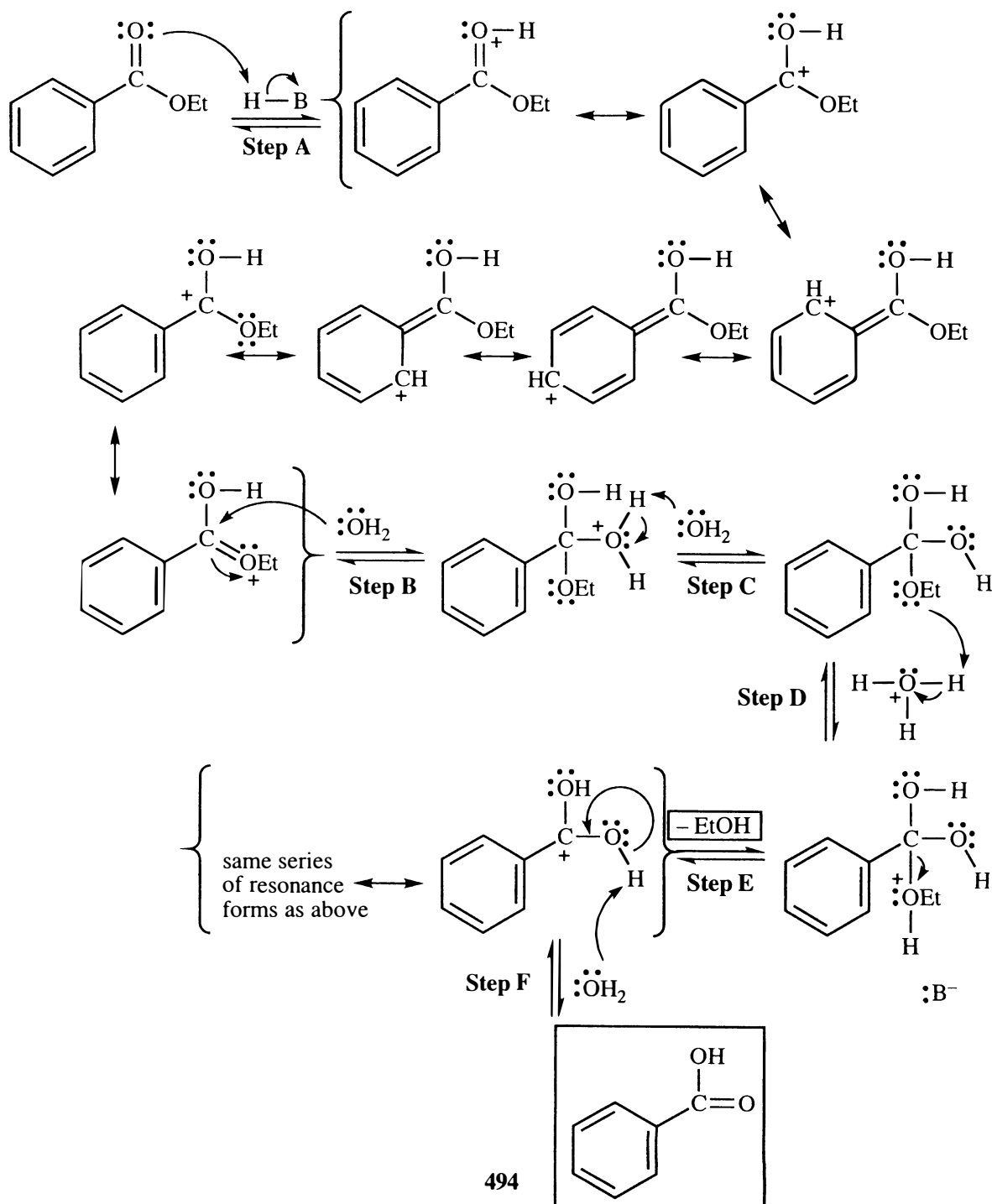
Step D proton on

Step E leaving group leaves (resonance stabilization)

Step F proton off

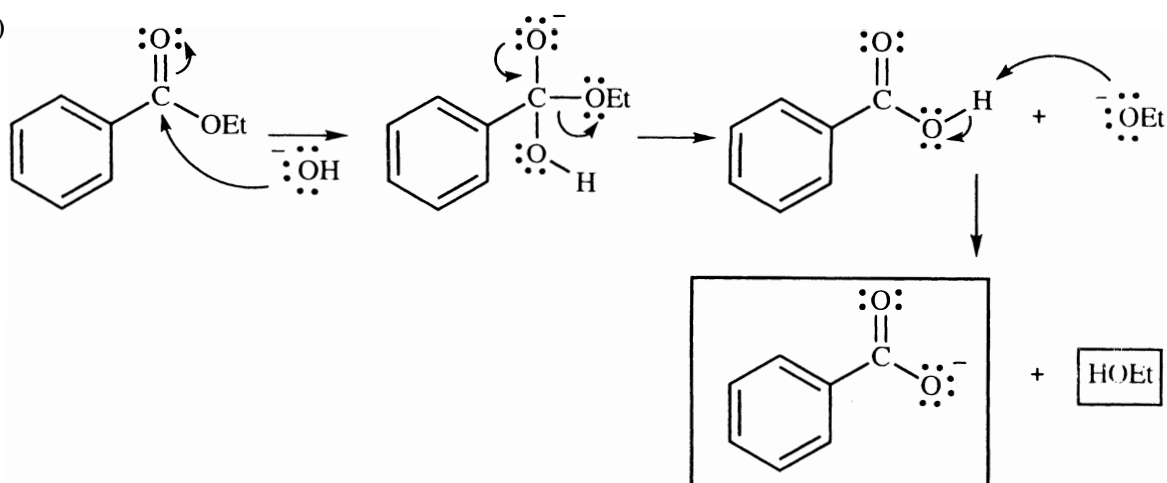
$\text{H}-\text{B}$ is the acid catalyst

$:\text{B}^-$ is the conjugate base, although in hydrolysis reactions, water usually removes H^+

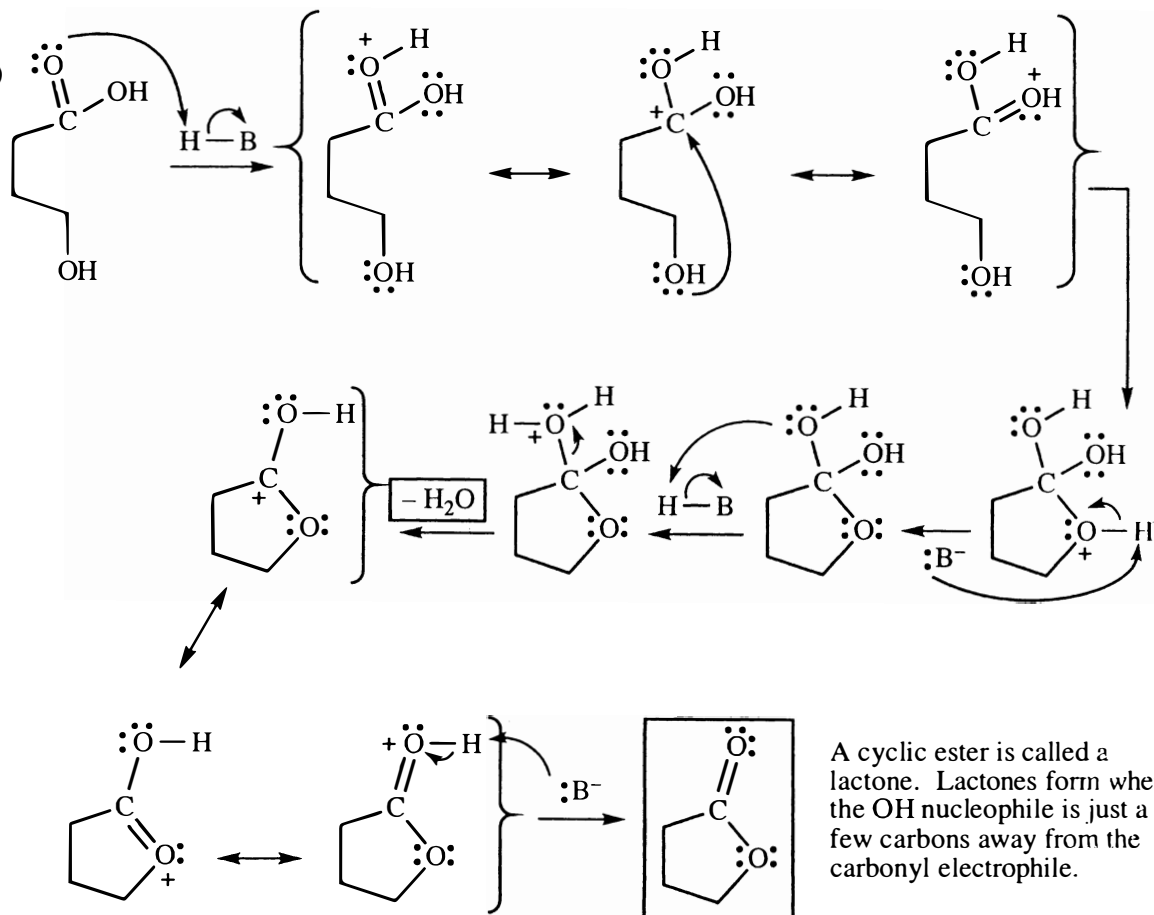


20-47 continued

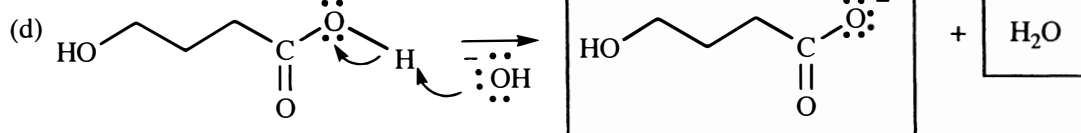
(b)



(c)



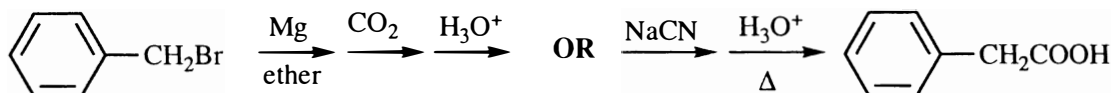
20-47 continued



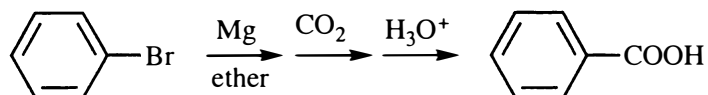
Esters can be formed only in acid, not in base.

20-48 Cyanide substitution is an S_N2 reaction and requires a 1° or 2° carbon with a leaving group. The Grignard reaction is less particular about the type of halide, but is sensitive to, and incompatible with, acidic functional groups and other reactive groups.

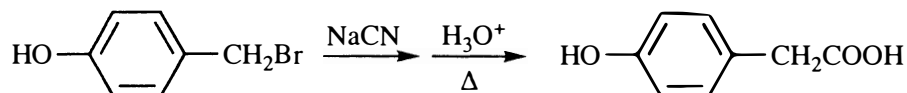
(a) Both methods will work.



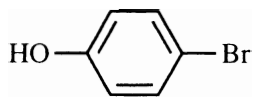
(b) Only Grignard will work. The S_N2 reaction does not work on unactivated benzene rings.



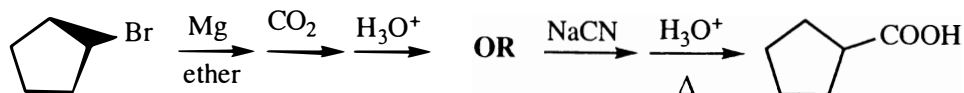
(c) Grignard will fail because of the OH group. The cyanide reaction will work, although an excess of cyanide will need to be added because the first equivalent will deprotonate the phenol.*



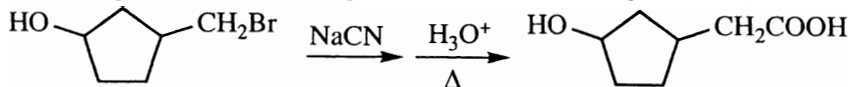
(d) Grignard will fail because of the OH group. The cyanide reaction will fail because S_N2 does not work on unactivated sp^2 carbons. In this case, NEITHER method will work.



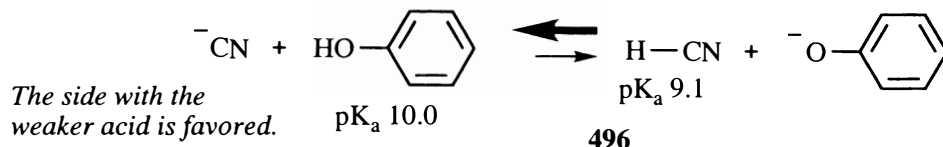
(e) Both methods will work, although cyanide substitution on 2° C will be accompanied by elimination.



(f) Grignard will fail because of the OH group. The cyanide reaction will work. Since alcohols are much less acidic than phenols, there is no problem with cyanide deprotonating the alcohol.*



* The pK_a of HCN is 9.1, and the pK_a of phenol is 10.0. Thus cyanide is strong enough to pull off some of the H from the phenol, although the equilibrium would favor cyanide ion and phenol. The pK_a of secondary alcohols is 16-18, so there is no chance that cyanide would deprotonate an alcohol.



20-50

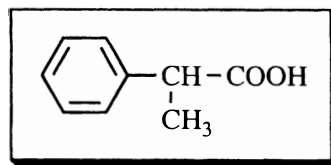
Spectrum A: $C_9H_{10}O_2 \Rightarrow$ 5 elements of unsaturation

δ 11.8, 1H $\Rightarrow$ COOH

δ 7.3, 5H $\Rightarrow$ monosubstituted benzene ring

δ 3.8, 1H quartet $\Rightarrow$ CHCH₃

δ 1.6, 3H doublet $\Rightarrow$ CHCH₃



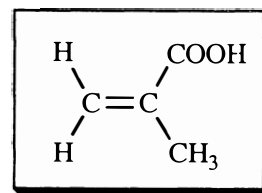
Spectrum B: $C_4H_6O_2 \Rightarrow$ 2 elements of unsaturation

δ 12.1, 1H $\Rightarrow$ COOH

δ 6.2, 1H singlet $\Rightarrow$ H—C=C

δ 5.7, 1H singlet $\Rightarrow$ H—C=C

δ 1.9, 3H singlet $\Rightarrow$ vinyl CH₃ with no H neighbors CH₃—C=C



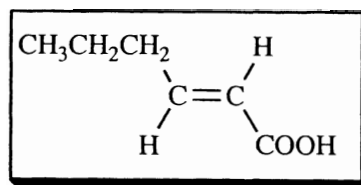
Spectrum C: $C_6H_{10}O_2 \Rightarrow$ 2 elements of unsaturation

δ 12.0, 1H $\Rightarrow$ COOH

δ 7.0, 1H multiplet $\Rightarrow$ H—C=C—COOH
 H

δ 5.7, 1H doublet $\Rightarrow$ C=C—COOH
 H

δ 2.2-0.8 $\Rightarrow$ CH₂CH₂CH₃



must be *trans* due to large coupling constant in doublet at δ 5.7

CHAPTER 21—CARBOXYLIC ACID DERIVATIVES

21-1 IUPAC name first; then common name

- (a) isobutyl benzoate (both IUPAC and common)
- (b) phenyl methanoate; phenyl formate
- (c) methyl 2-phenylpropanoate; methyl α -phenylpropionate
- (d) *N*-phenyl-3-methylbutanamide; β -methylbutyranilide
- (e) *N*-benzylethanamide; *N*-benzylacetamide
- (f) 3-hydroxybutanenitrile; β -hydroxybutyronitrile
- (g) 3-methylbutanoyl bromide; isovaleryl bromide
- (h) dichloroethanoyl chloride; dichloroacetyl chloride
- (i) 2-methylpropanoic methanoic anhydride; isobutyric formic anhydride
- (j) cyclopentyl cyclobutanecarboxylate (both IUPAC and common)
- (k) 5-hydroxyhexanoic acid lactone; δ -caprolactone
- (l) *N*-cyclopentylbenzamide (both IUPAC and common)
- (m) propanedioic anhydride; malonic anhydride
- (n) 1-hydroxycyclopentanecarbonitrile; cyclopentanone cyanohydrin
- (o) *cis*-4-cyanocyclohexanecarboxylic acid; no common name
- (p) 3-bromobenzoyl chloride; *m*-bromobenzoyl chloride
- (q) *N*-methyl-5-aminoheptanoic acid lactam; no common name
- (r) *N*-ethanoylpiperidine; *N*-acetylpiperidine

21-2 An aldehyde has a C—H absorption (usually 2 peaks) at $2700\text{--}2800\text{ cm}^{-1}$. A carboxylic acid has a strong, broad absorption between $2400\text{--}3400\text{ cm}^{-1}$. The spectrum of methyl benzoate has no peaks in this region.

21-3 The C—O single bond stretch in ethyl octanoate appears at 1170 cm^{-1} , while methyl benzoate shows this absorption at 1120 and 1280 cm^{-1} .

21-4

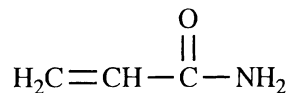
- (a) acid chloride: single C=O peak at 1800 cm^{-1} ; no other carbonyl comes so high
- (b) primary amide: C=O at 1650 cm^{-1} and two N—H peaks between $3200\text{--}3400\text{ cm}^{-1}$
- (c) anhydride: two C=O absorptions at 1750 and 1820 cm^{-1}

21-5

(a) The formula $\text{C}_3\text{H}_5\text{NO}$ has two elements of unsaturation. The IR spectrum shows two peaks between $3200\text{--}3400\text{ cm}^{-1}$, an NH_2 group. The strong peak at 1670 cm^{-1} is a C=O, and the peak at 1610 cm^{-1} is a C=C. This accounts for all of the atoms.

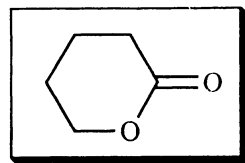
The ^1H NMR corroborates the assignment. The ^1H multiplet at δ 5.8 is the vinyl H next to the carbonyl. The ^2H multiplet at δ 6.3 is the vinyl hydrogen pair on carbon-3. The ^2H singlet at δ 4.8 is the amide hydrogens.

The ^{13}C NMR confirms the structure: two vinyl carbons and a carbonyl.



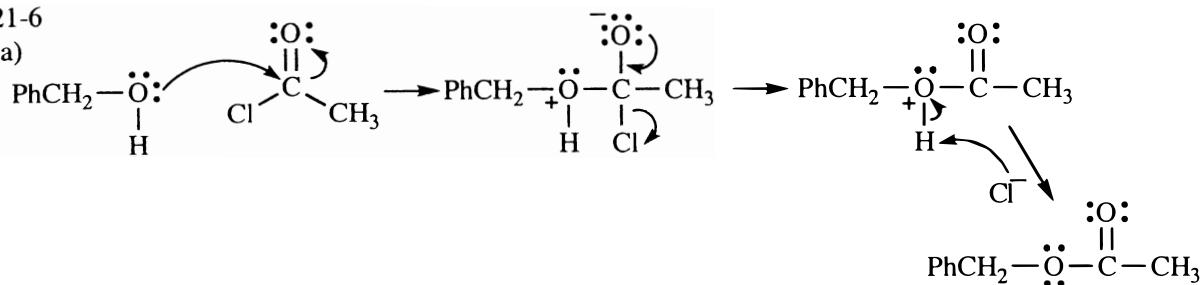
(b) The formula $\text{C}_5\text{H}_8\text{O}_2$ has two elements of unsaturation. The IR spectrum shows no significant OH, so this compound is neither an alcohol nor a carboxylic acid. The strong peak at 1730 cm^{-1} is likely an ester carbonyl. The C—O appears between $1050\text{--}1250\text{ cm}^{-1}$. The IR shows no C=C absorption, so the other element of unsaturation is likely a ring. The carbon NMR spectrum shows the carbonyl carbon at δ 171, the C—O carbon at δ 69, and three more carbons in the aliphatic region, but no carbons in the vinyl region between δ 100–150, so there can be no C=C. The proton NMR shows multiplets of 2H at δ 4.3 and 2.5, most likely CH_2 groups next to oxygen and carbonyl respectively.

The only structure with an ester, four CH_2 groups, and a ring, is δ -valerolactone:

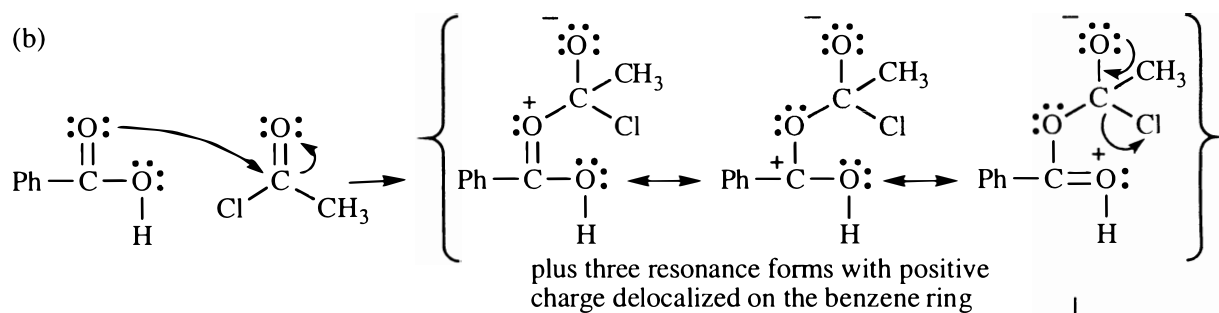


21-6

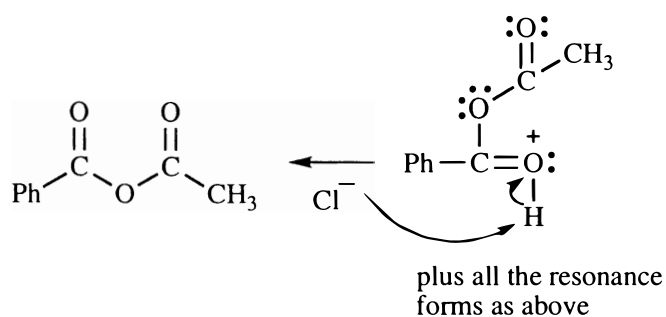
(a)



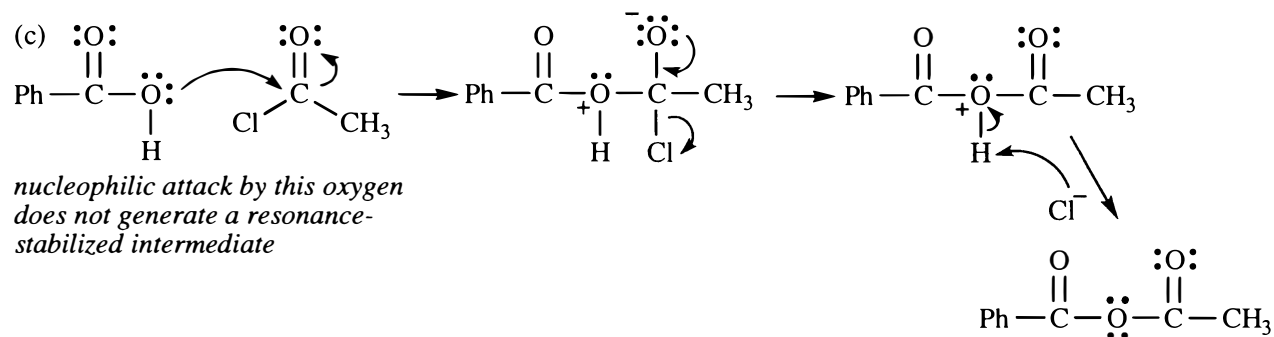
(b)



the carbonyl oxygen is more nucleophilic than the single-bonded oxygen because the product is resonance stabilized

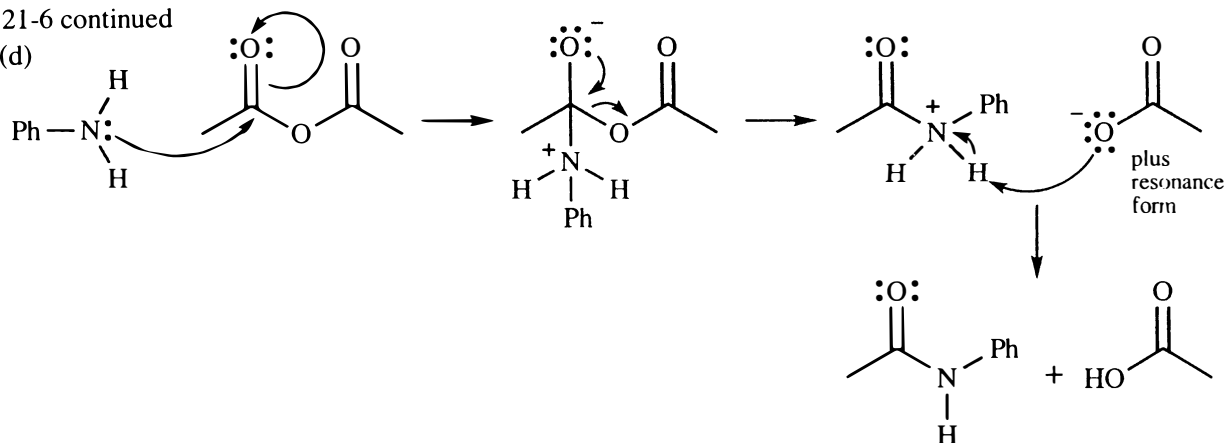


(c)

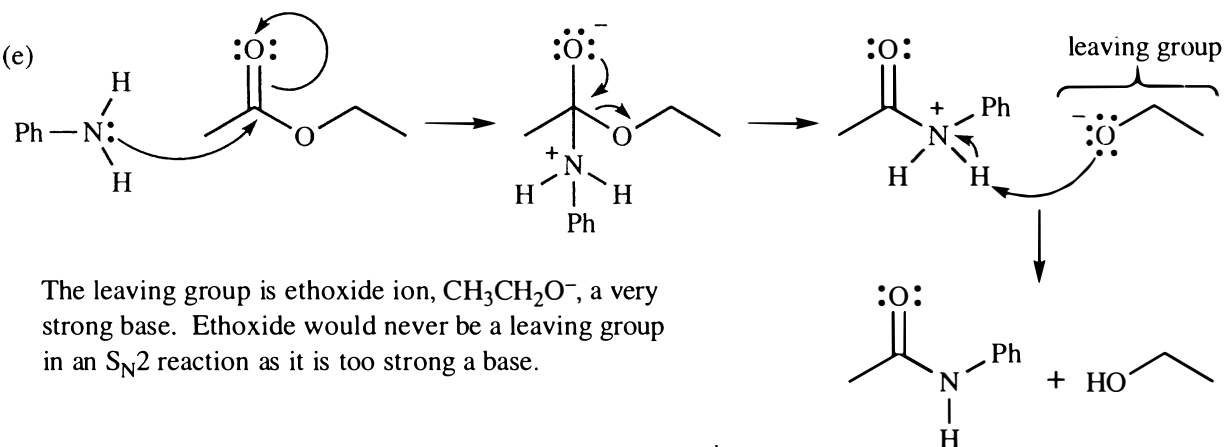


21-6 continued

(d)



(e)



The leaving group is ethoxide ion, $\text{CH}_3\text{CH}_2\text{O}^-$, a very strong base. Ethoxide would never be a leaving group in an $\text{S}_{\text{N}}2$ reaction as it is too strong a base.

21-7 **Figure 21-9 is critical!** Reactions which go from a more reactive functional group to a less reactive functional group ("downhill reactions") will occur readily.

(a) amide to acid chloride will NOT occur—it is an "uphill" transformation

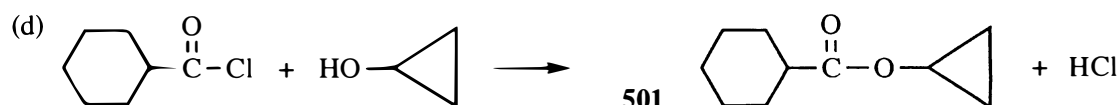
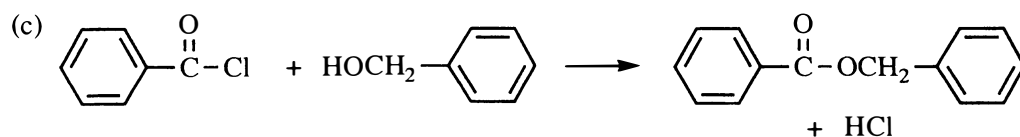
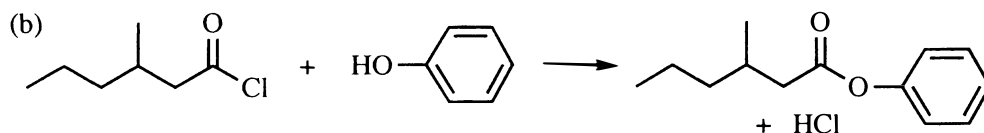
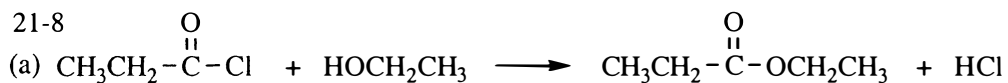
(b) acid chloride to amide will occur rapidly

(c) amide to ester will NOT occur—another "uphill" transformation

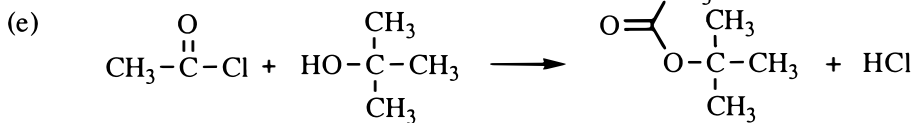
(d) acid chloride to anhydride will occur rapidly

(e) anhydride to amide will occur rapidly

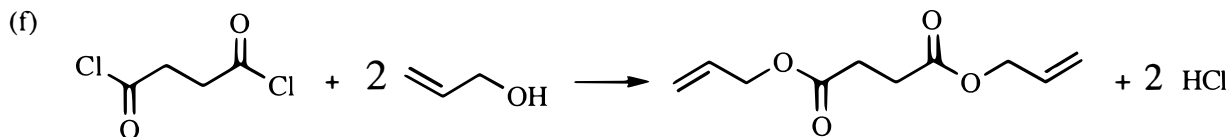
21-8



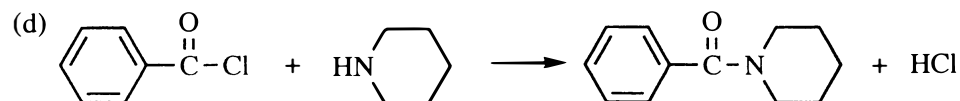
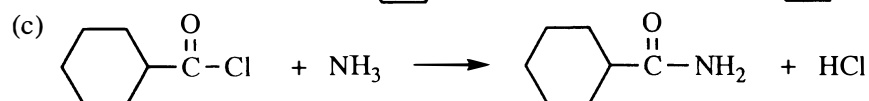
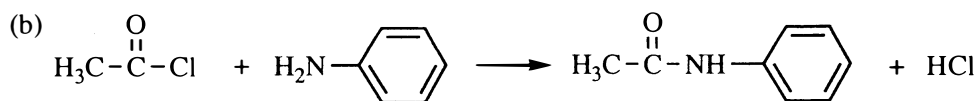
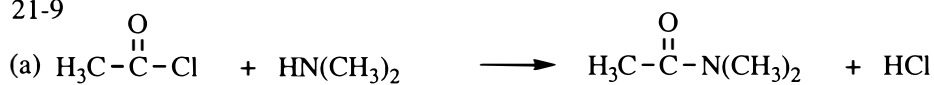
21-8 continued



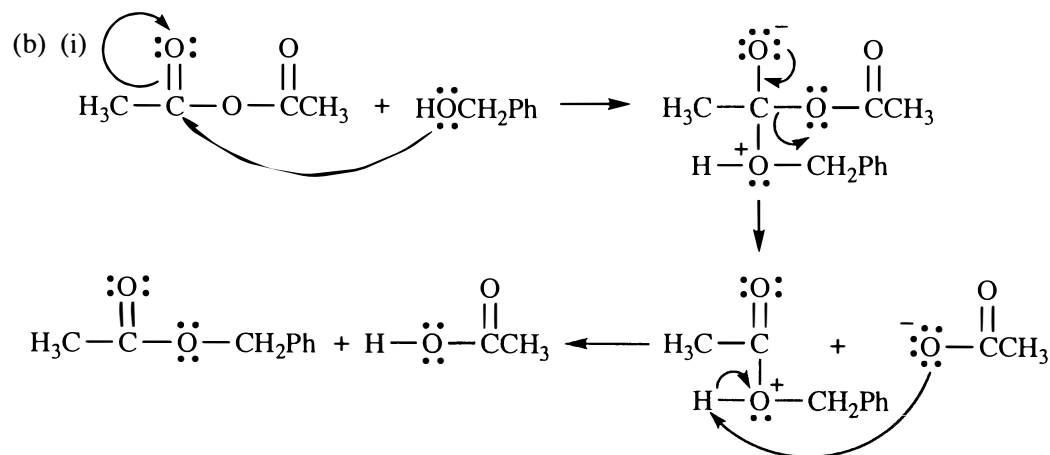
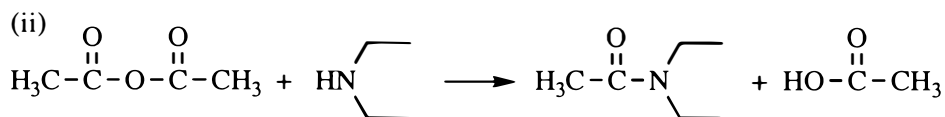
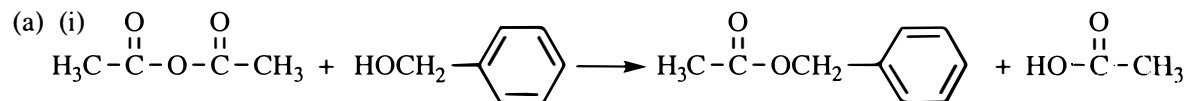
This reaction would have to be kept cold to avoid elimination. Esters of *t*-butyl alcohol are hard to make.



21-9

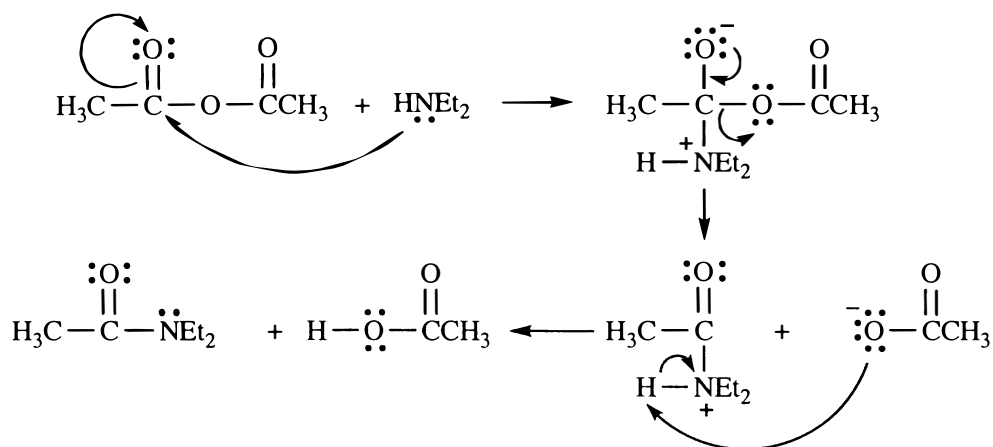


21-10

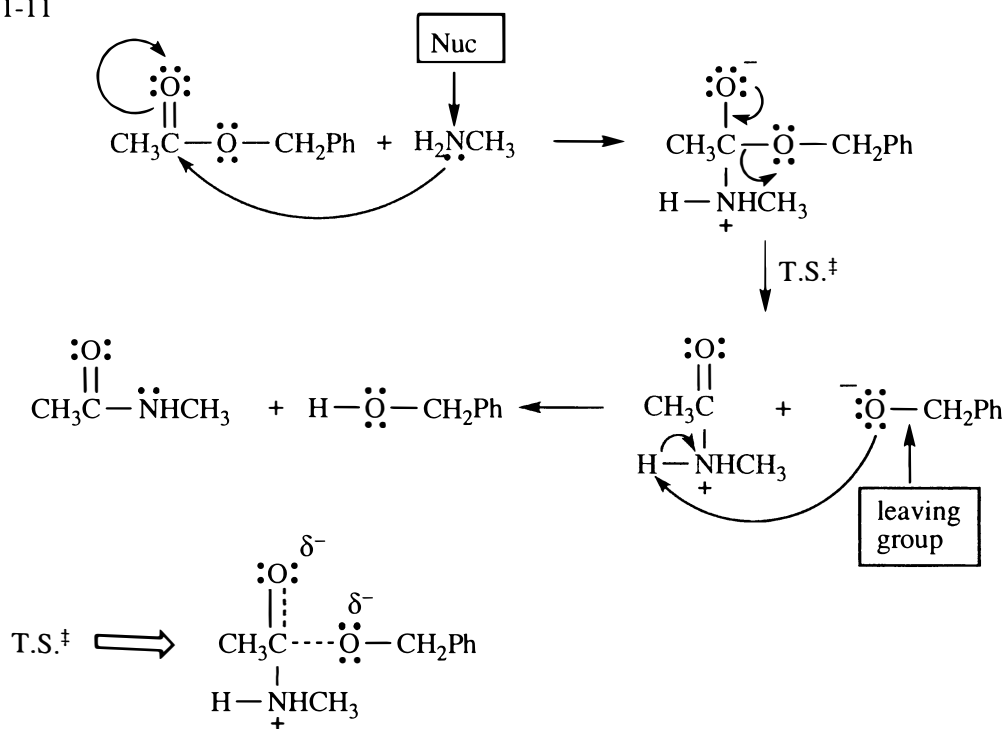


21-10 (b) continued

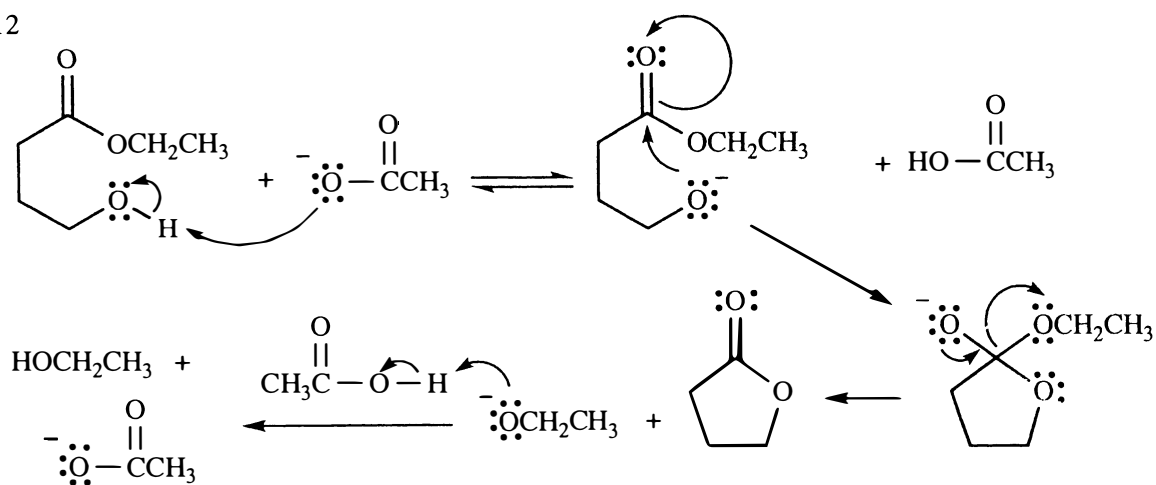
(ii)



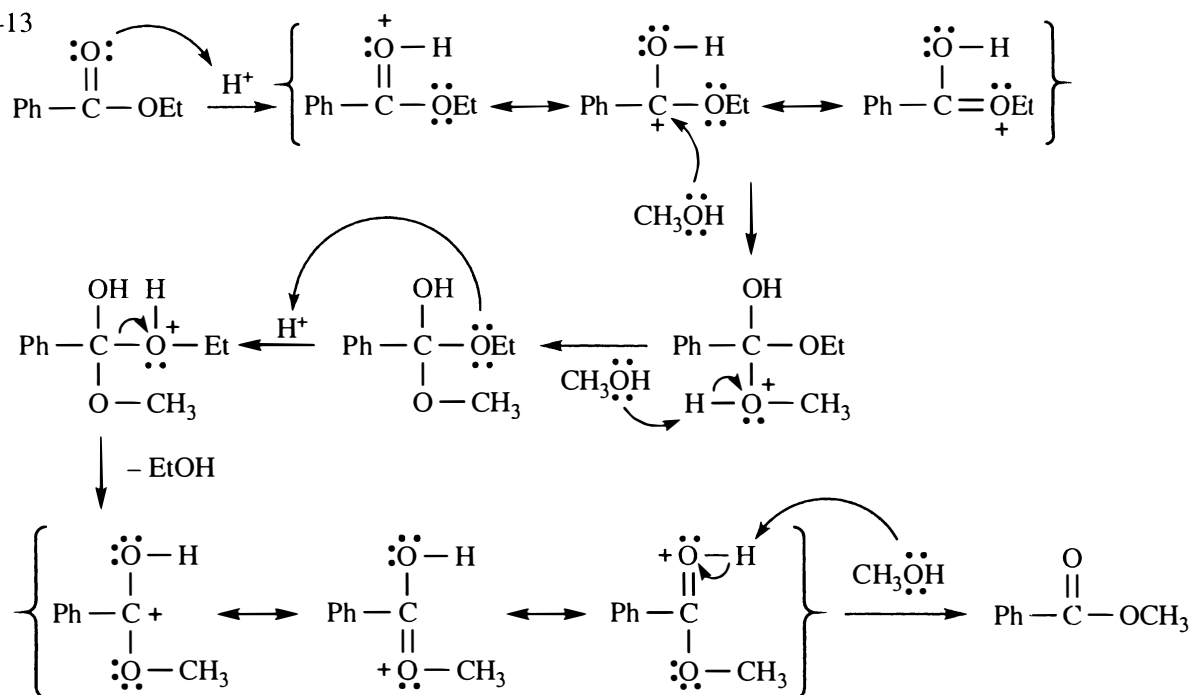
21-11

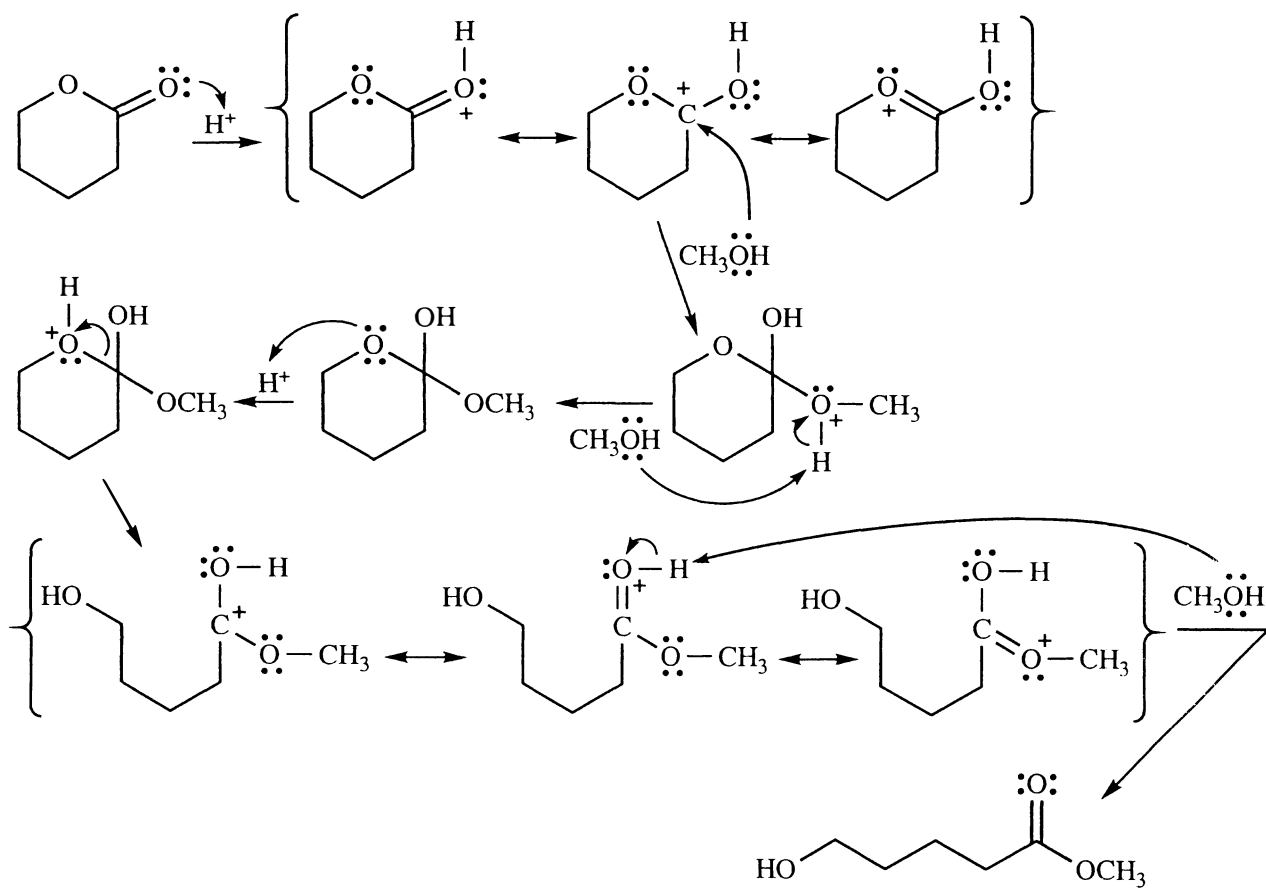


21-12

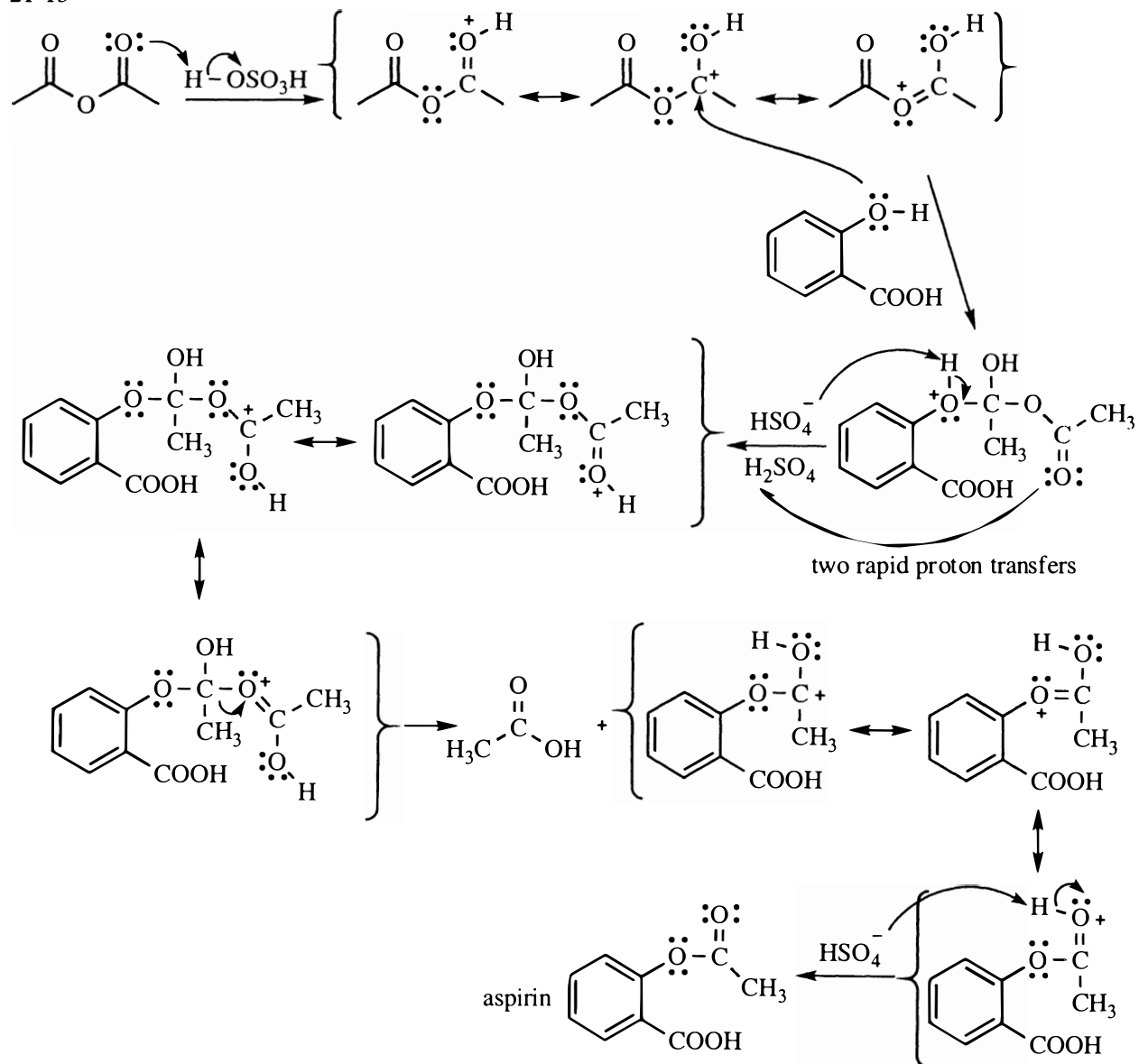


21-13





21-15



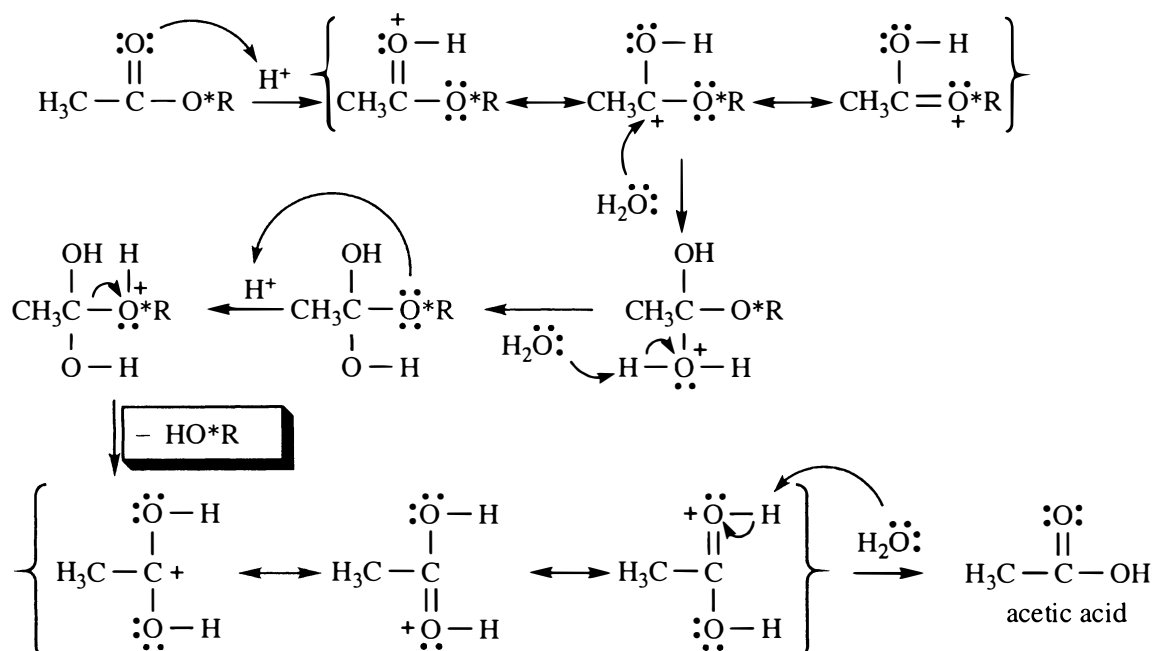
(a)

$$\text{H}_3\text{C}-\text{C}(=\text{O})-\text{O}^*\text{R} + \text{:}\ddot{\text{O}}\text{H}^- \longrightarrow \text{H}_3\text{C}-\text{C}(\text{O}^-)(\text{OH})-\text{O}^*\text{R} \longrightarrow \text{H}_3\text{C}-\text{C}(=\text{O})-\text{O}^- + \text{:}\ddot{\text{O}}^*\text{R}^- \longrightarrow \text{H}_3\text{C}-\text{C}(=\text{O})-\text{O}^- + \text{H}-\text{O}^*\text{R}$$

$$\text{O}^*\text{R} = \begin{array}{c} \text{CH}_2\text{CH}_3 \\ | \\ \text{R}-\text{C}-\text{H} \\ | \\ \text{CH}_3 \end{array}$$

$$\text{H}-\text{O}^*\text{R} = \begin{array}{c} \text{CH}_2\text{CH}_3 \\ | \\ \text{H}^{18}\text{O}-\text{C}-\text{H} \\ | \\ \text{CH}_3 \end{array}$$

(b) The products are identical regardless of mechanism.



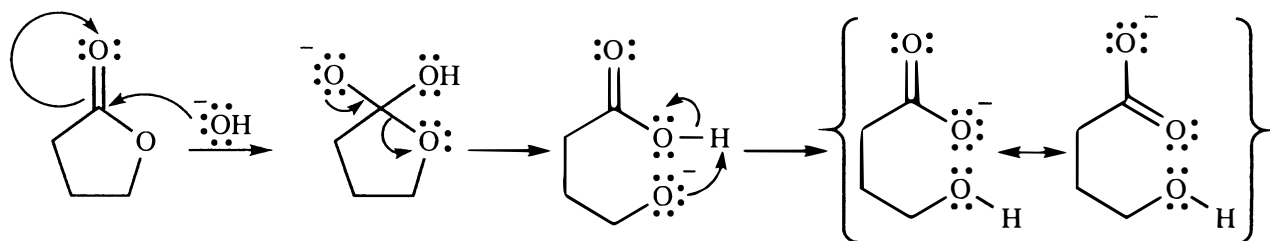
To show if the alcohol was chiral or racemic, measuring its optical activity in a polarimeter and comparing to known values would prove its configuration. (The heavy oxygen isotope has a negligible effect on optical rotation.)

21-17

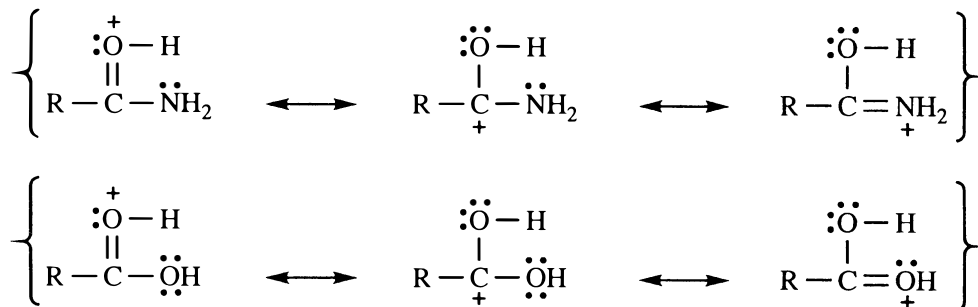
(a) A catalyst is defined as a chemical species that speeds a reaction but is not consumed in the reaction. In the acidic hydrolysis, acid is used in the first and fourth steps of the mechanism but is regenerated in the third and last steps. Acid is not consumed; the final concentration of acid is the same as the initial concentration. In the basic hydrolysis, however, the hydroxide that initially attacks the carbonyl is never regenerated. An alkoxide leaves from the carbonyl, but it quickly neutralizes the carboxylic acid. For every molecule of ester, one molecule of hydroxide is consumed; the base *promotes* the reaction but does not *catalyze* the reaction.

(b) Basic hydrolysis is not reversible. Once an ester molecule is hydrolyzed in base, the carboxylate cannot form an ester. Acid catalysis, however, is an equilibrium: the mixture will always contain some ester, and the yield will never be as high as in basic hydrolysis. Second, long chain fatty acids are not soluble in water until they are ionized; they are soluble only as their sodium salts (soap). Basic hydrolysis is preferred for higher yield and greater solubility of the product.

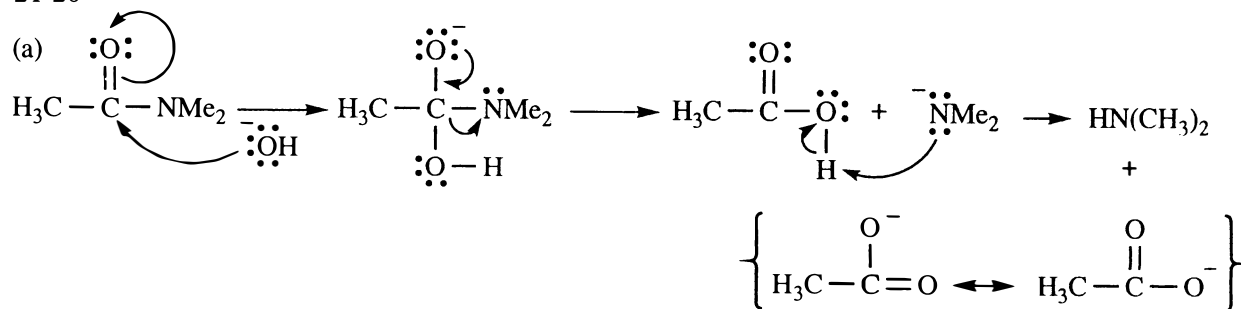
21-18



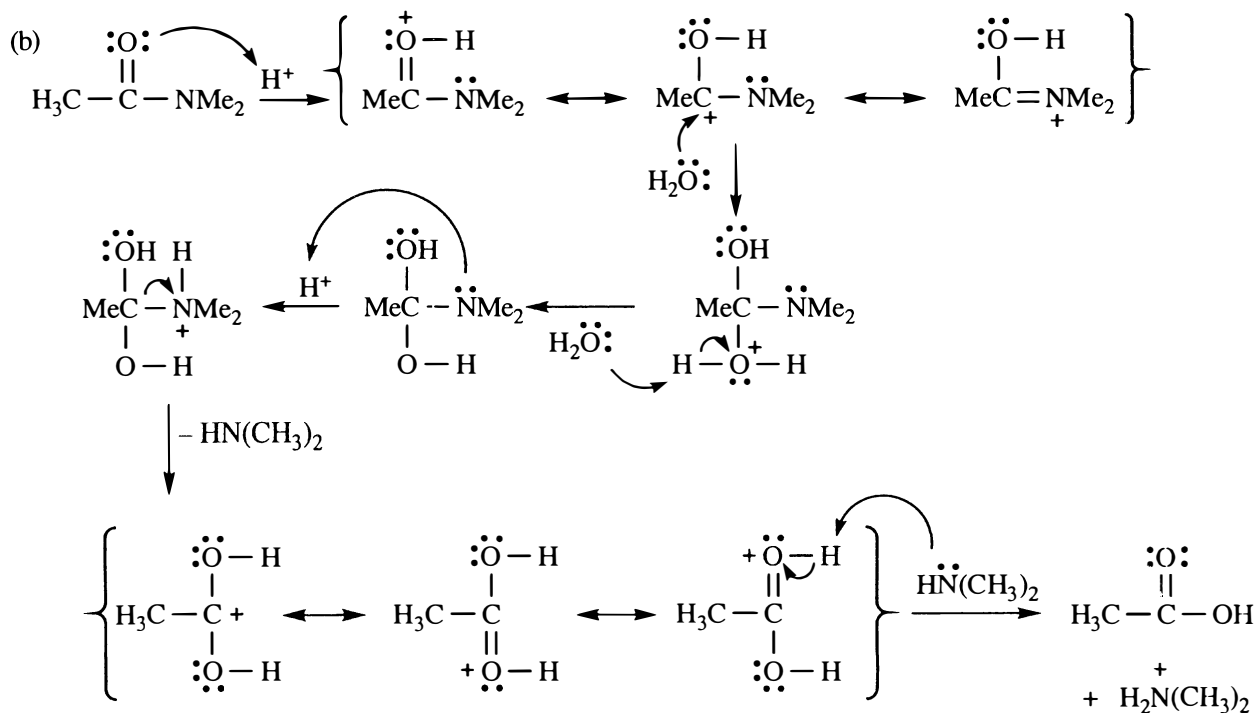
21-19



21-20

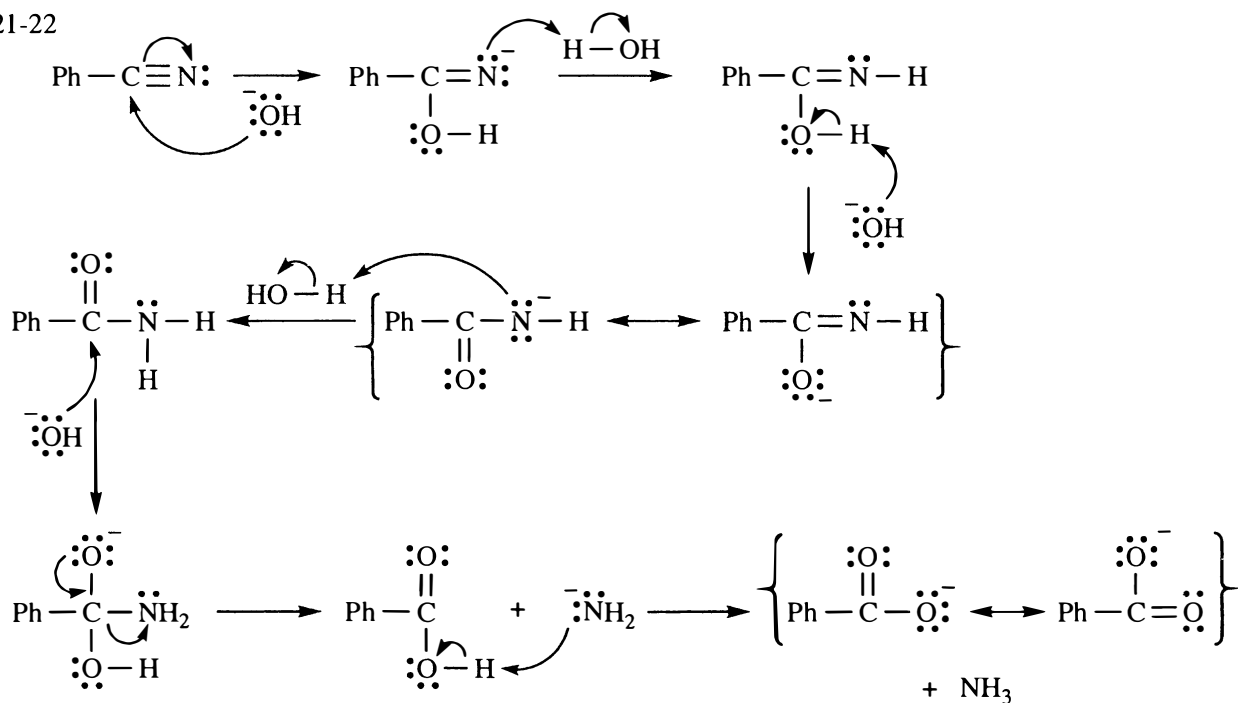


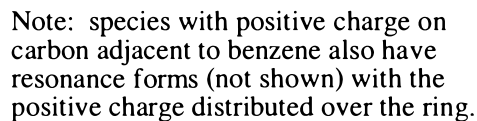
21-20 continued



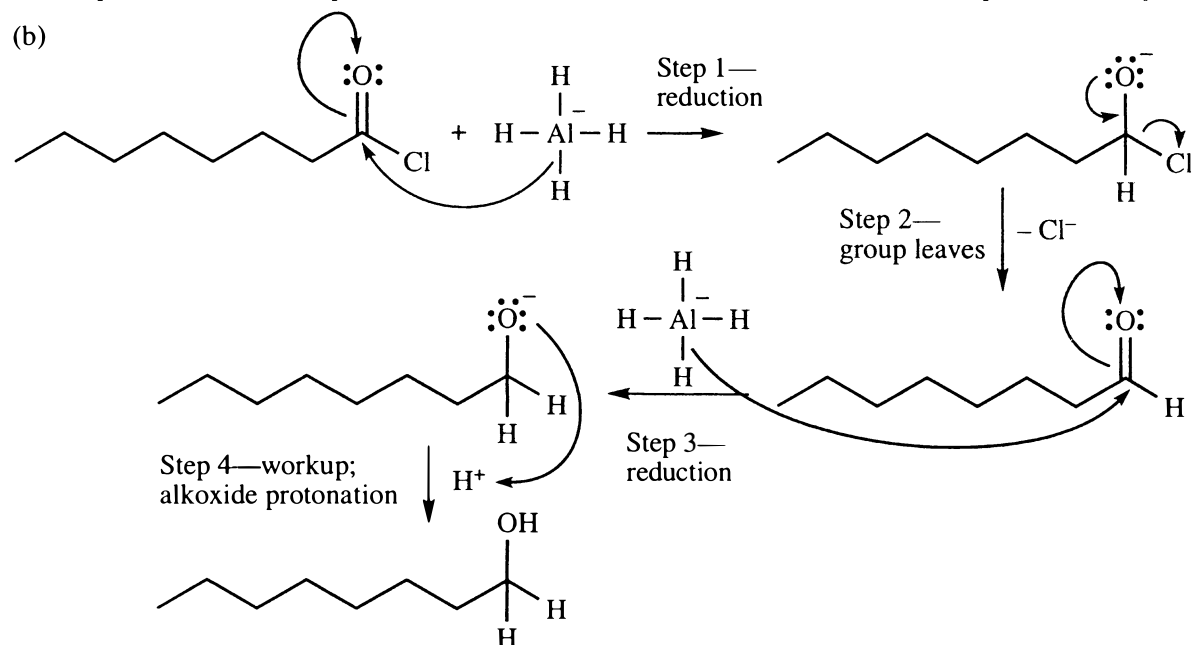
21-21 In the basic hydrolysis (21-20(a)), the step that drives the reaction to completion is the final step, the deprotonation of the carboxylic acid by the amide anion. In the acidic hydrolysis (21-20(b)), protonation of the amine by acid is exothermic and it prevents the reverse reaction by tying up the pair of electrons on the nitrogen so that the amine is no longer nucleophilic.

21-22

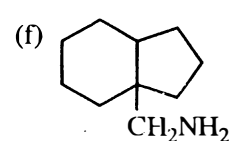
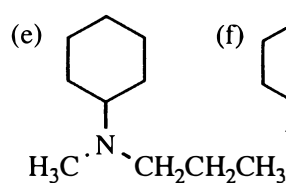
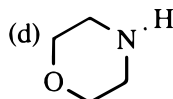
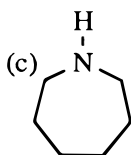
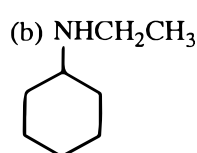


$$\text{Ph}-\text{C}\equiv\text{N}:\xrightarrow{\text{H}^+}\left\{\text{Ph}-\text{C}\equiv\overset{+}{\text{N}}-\text{H}\longleftrightarrow\text{Ph}-\overset{+}{\text{C}}=\ddot{\text{N}}-\text{H}\right\}$$


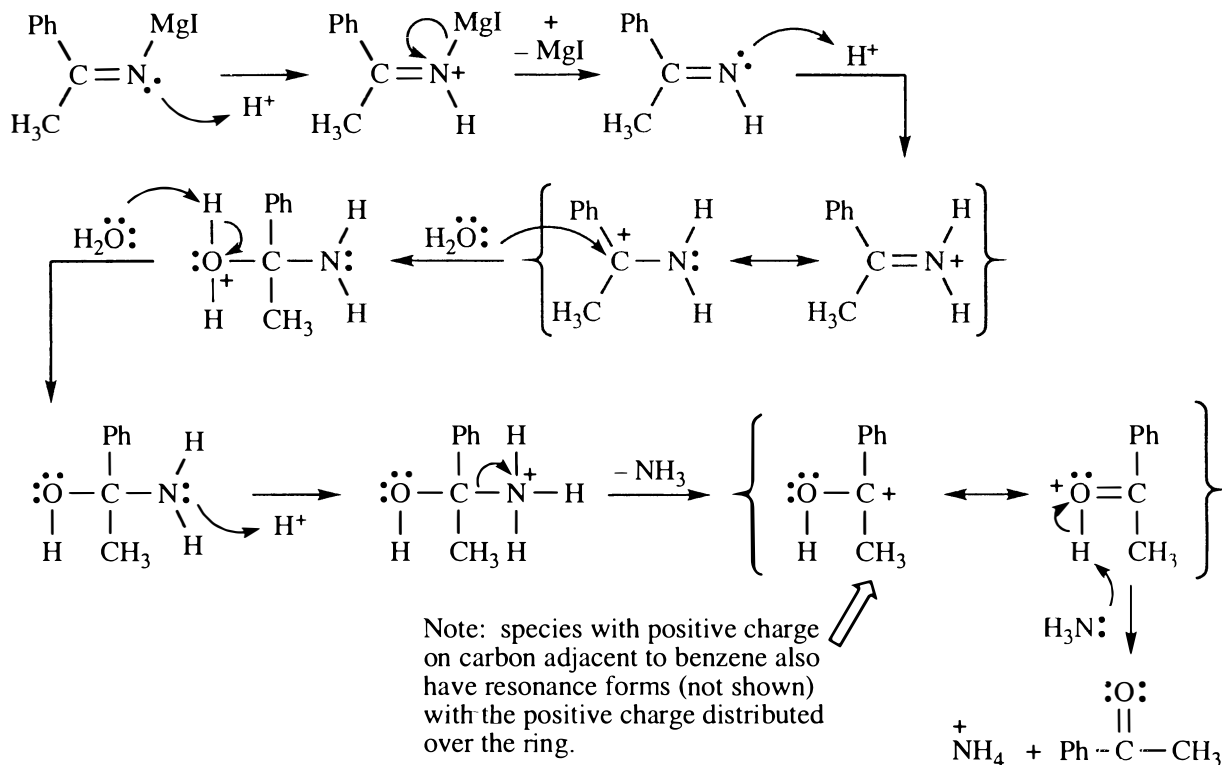
(a) Reduction occurs when a new C-H bond is formed. In ester reduction, a new C-H bond is formed in the first step and in the third step. This can also be seen in this mechanism where the steps are similarly labeled.



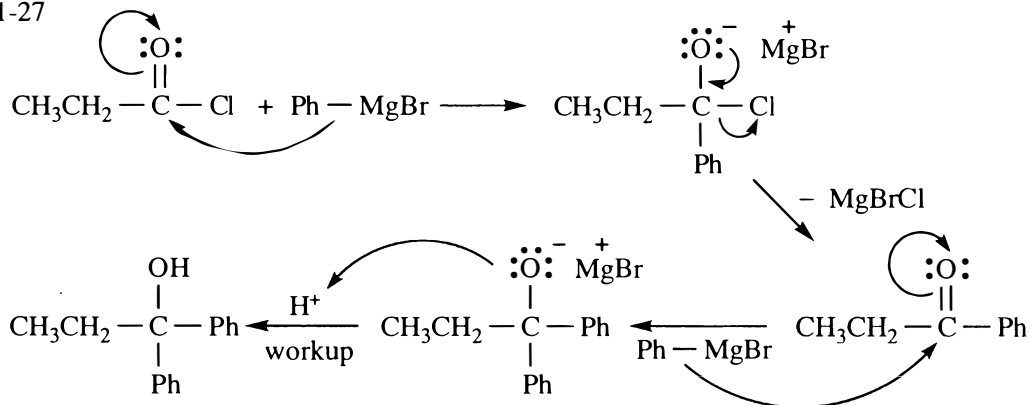
(a)

CCCN

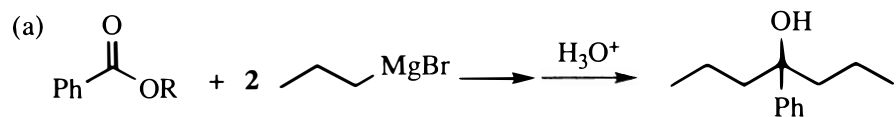
21-26



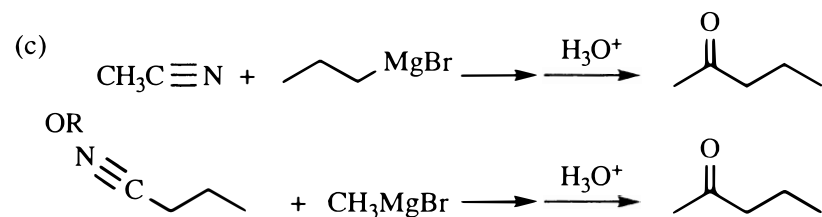
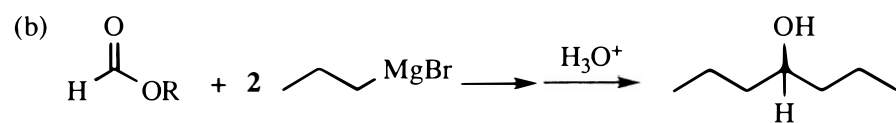
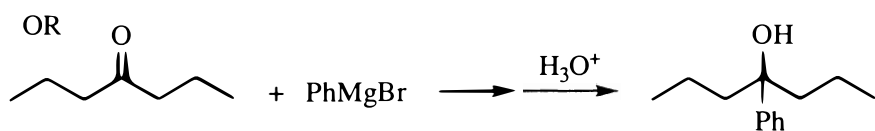
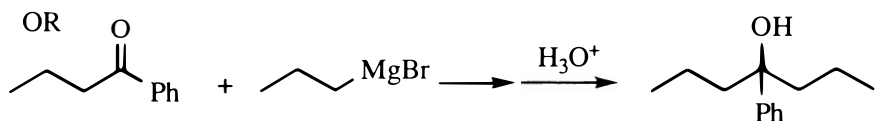
21-27



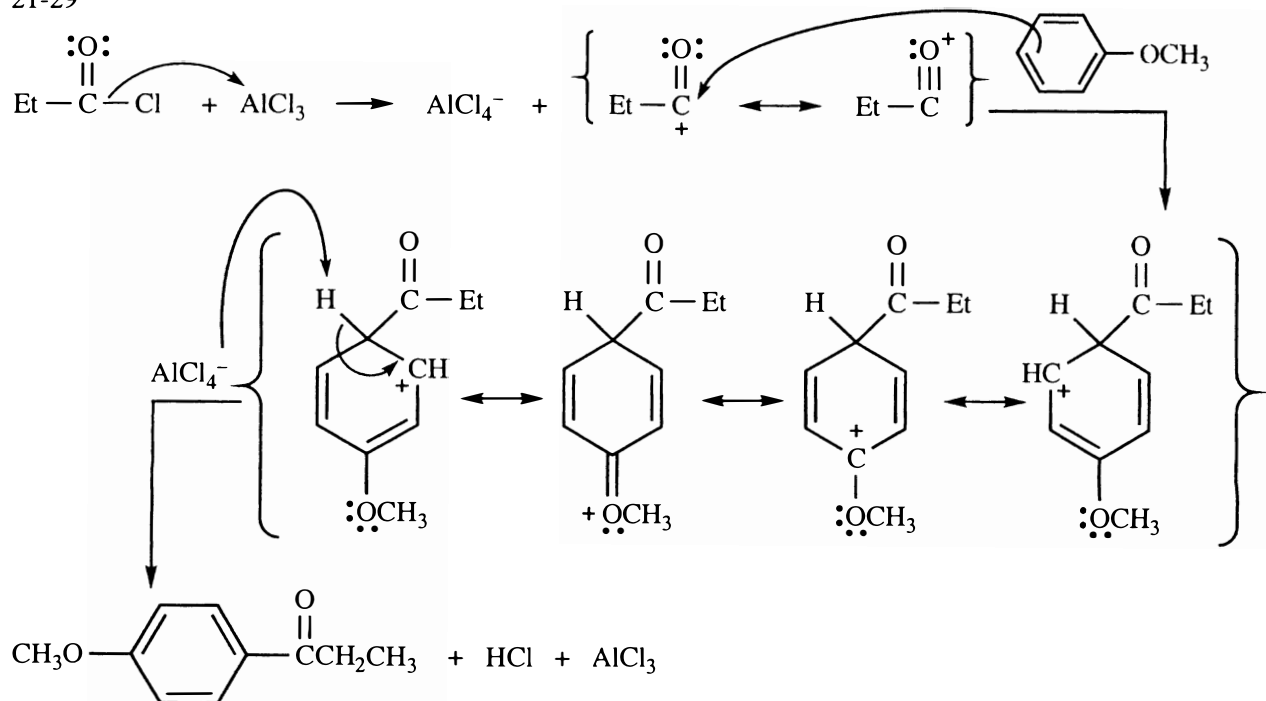
21-28



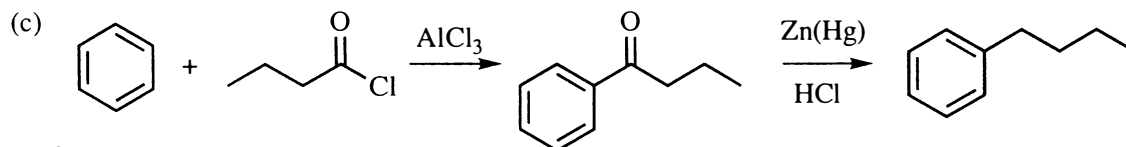
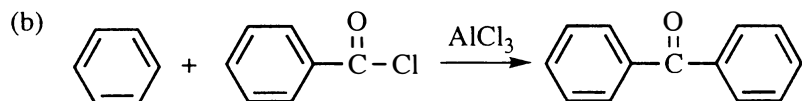
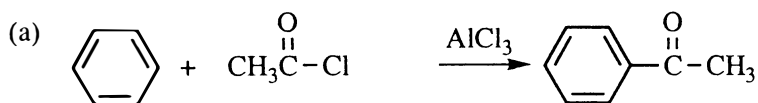
these alcohols can also be synthesized from ketones:



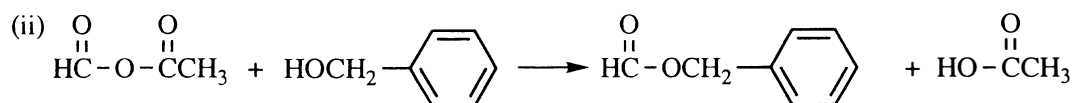
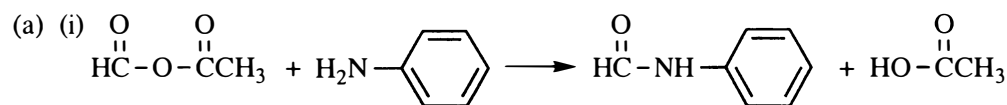
21-29



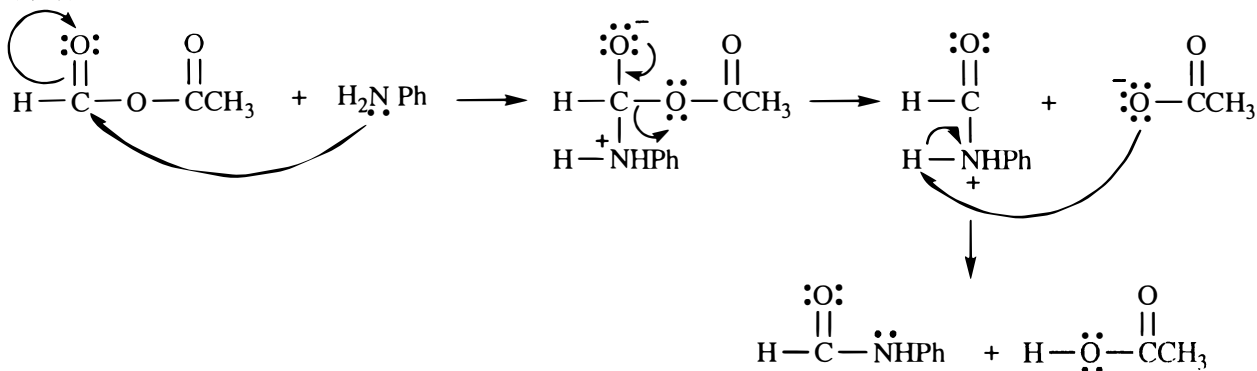
21-30



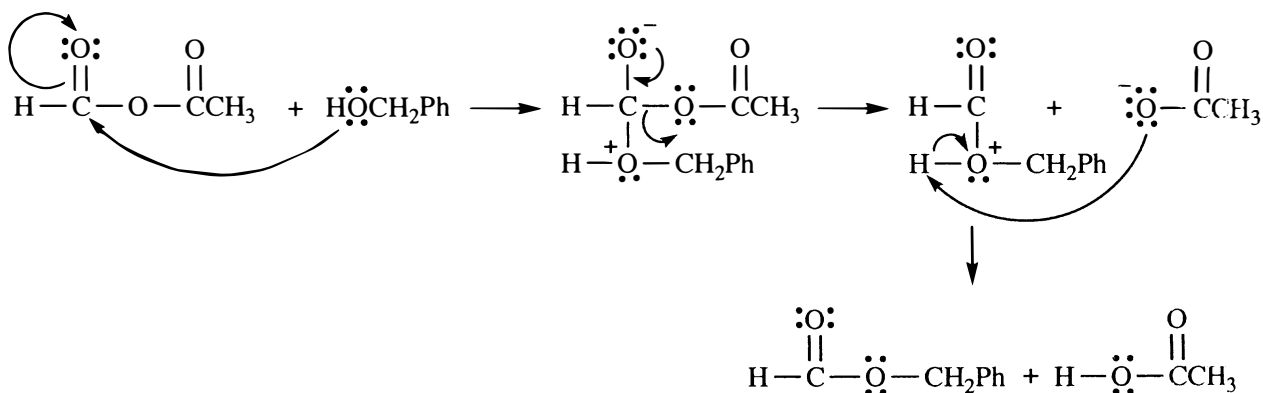
21-31



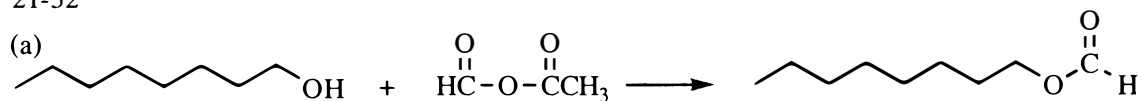
(b) (i)



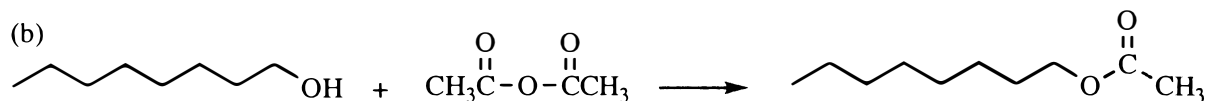
(ii)



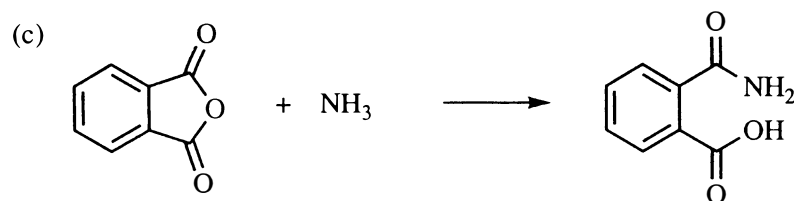
21-32



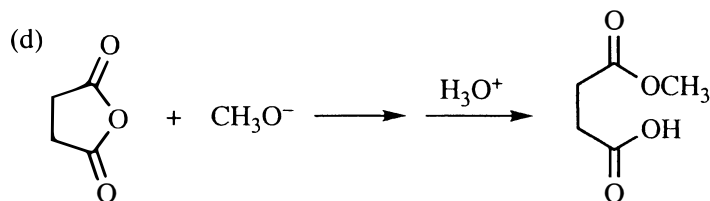
$\text{HC}-\text{Cl}$ does not exist, so acetic formic anhydride is the most practical way to formylate the alcohol.



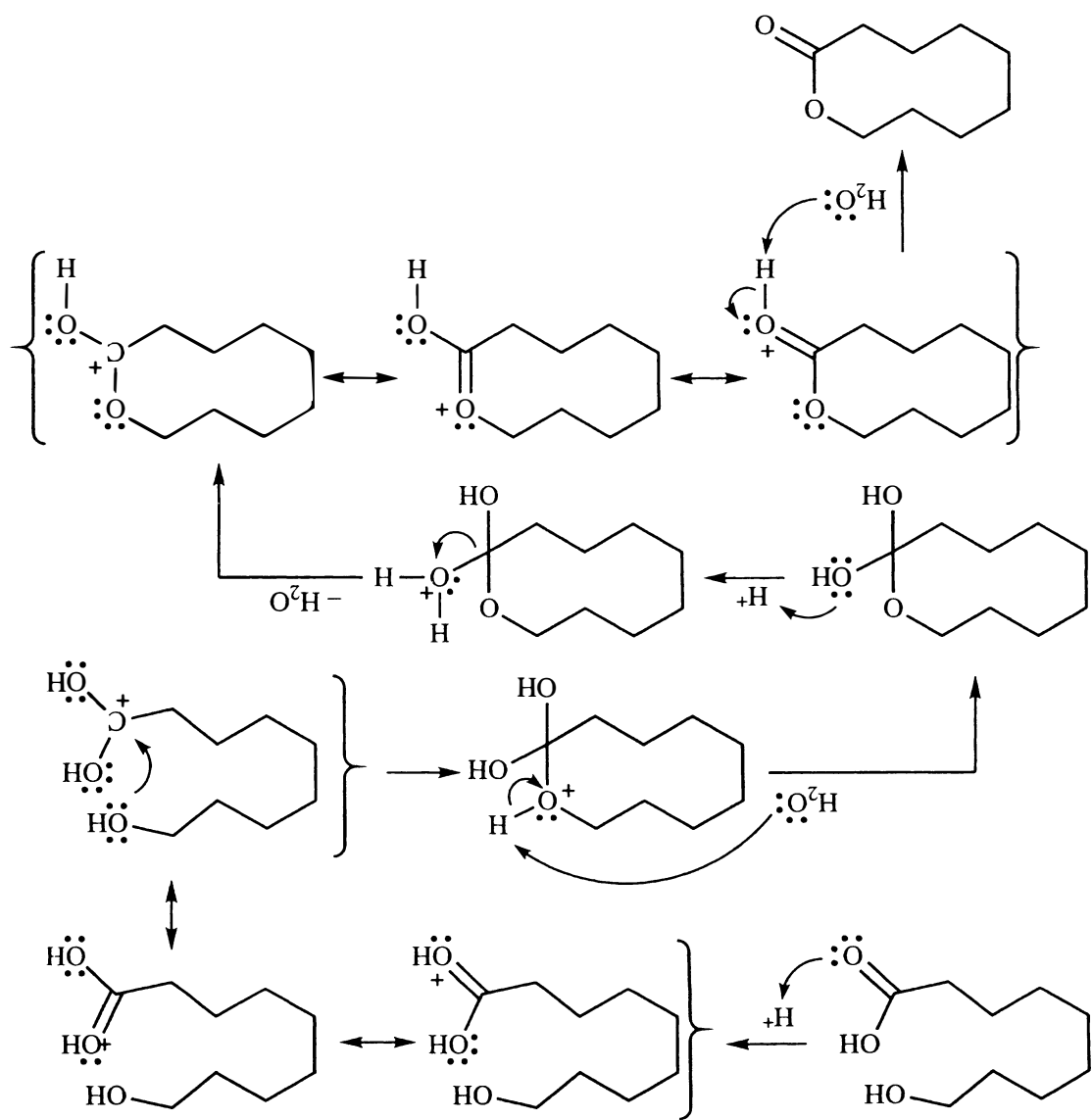
Acetic anhydride is more convenient and less expensive than acetyl chloride.



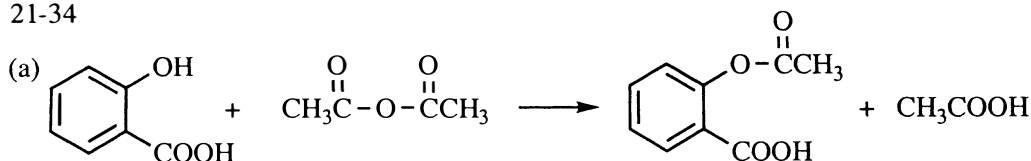
The acid chloride would tend to react at both carbonyls instead of just one; only the anhydride will give this product.



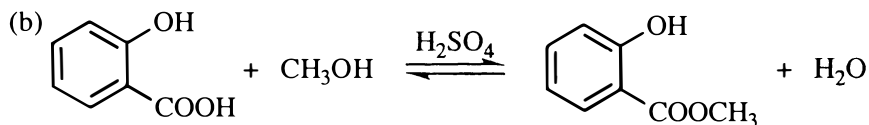
The acid chloride would tend to react at both carbonyls instead of just one; only the anhydride will give this product.



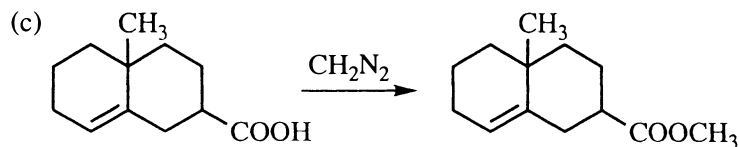
21-34



Generally, acetic anhydride is the optimum reagent for the preparation of acetate esters. Acetyl chloride would also react with the carboxylic acid to form a mixed anhydride.

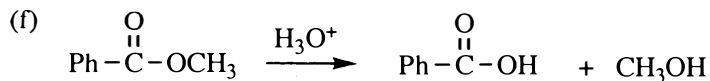
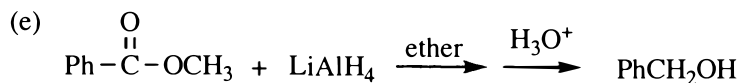
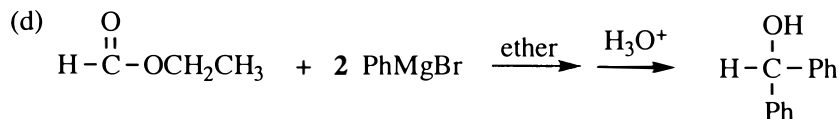
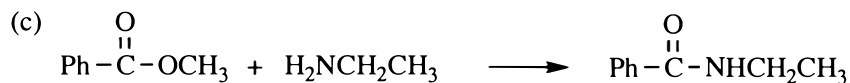
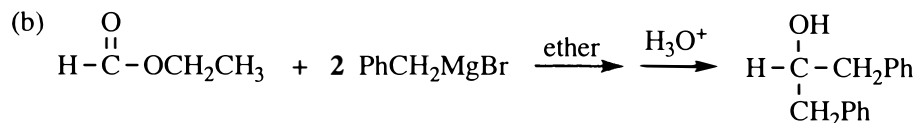
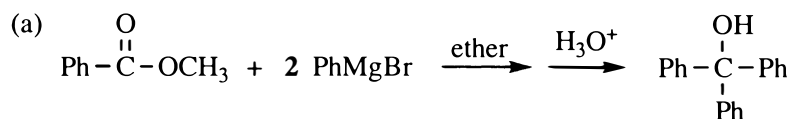


Fischer esterification works well to prepare simple carboxylic esters. The diazomethane method would also react with the phenol, making the phenyl ether.

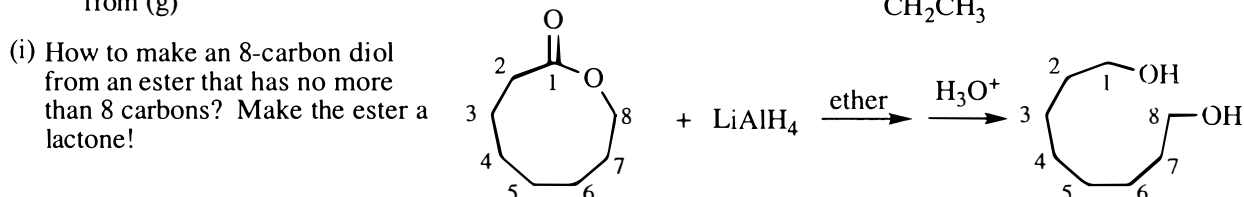
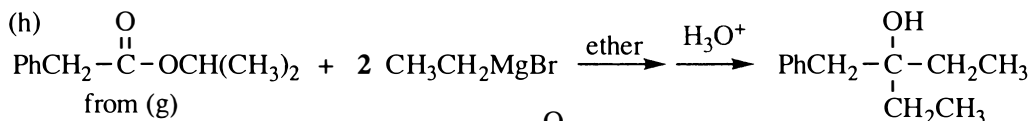
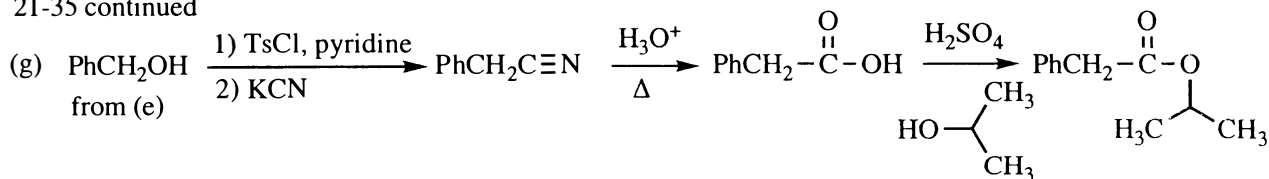


Fischer esterification would make the ester, but in the process, the acidic conditions would risk migrating the double bond into conjugation with the carbonyl group. The diazomethane reaction is run under neutral conditions where double bond migration will not occur.

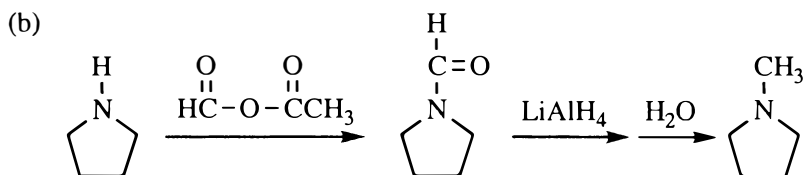
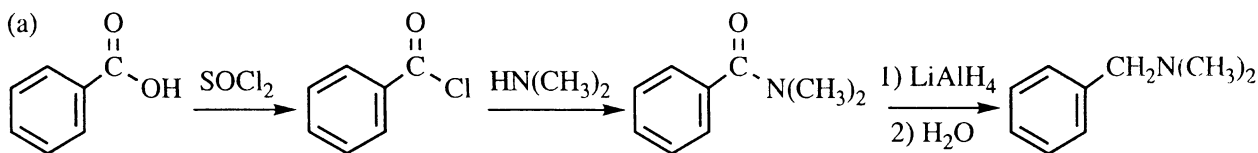
21-35 Syntheses may have more than one correct approach.



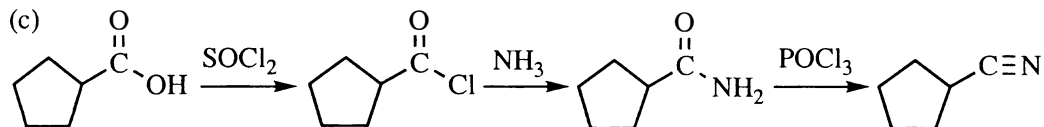
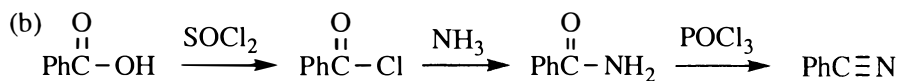
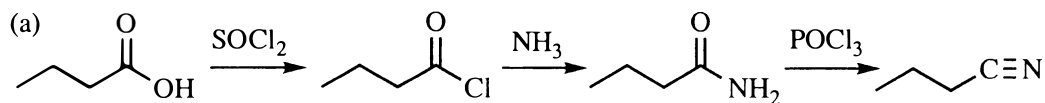
21-35 continued



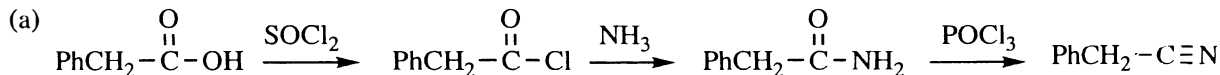
21-36 There may be additional correct approaches to these problems.



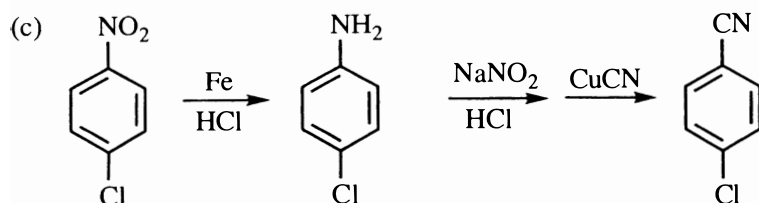
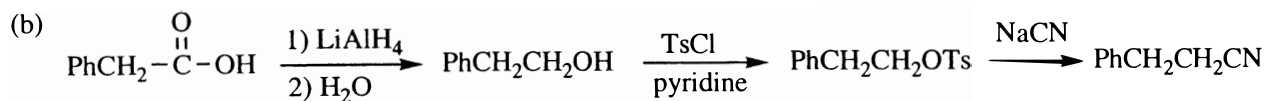
21-37 Prepare the amide, then dehydrate.



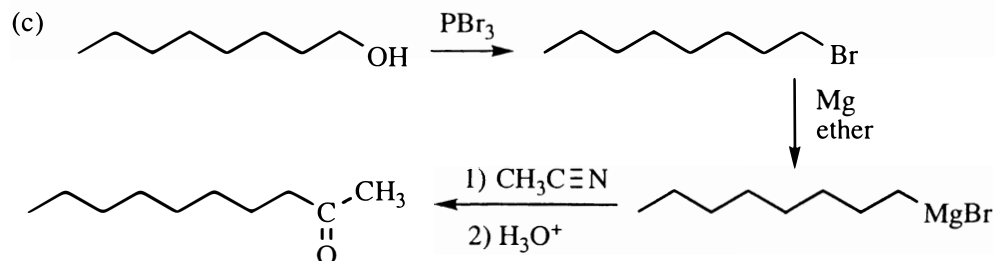
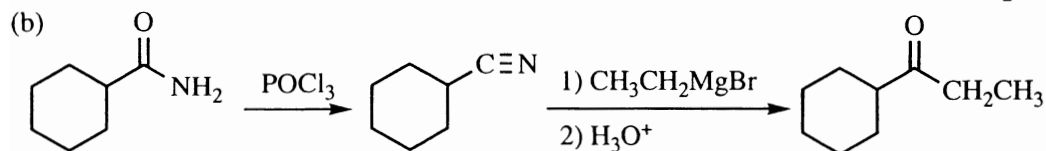
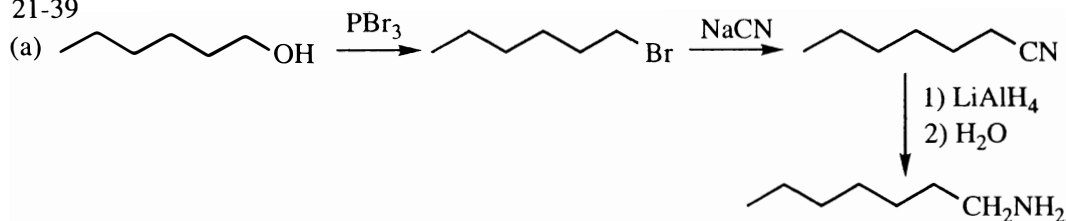
21-38



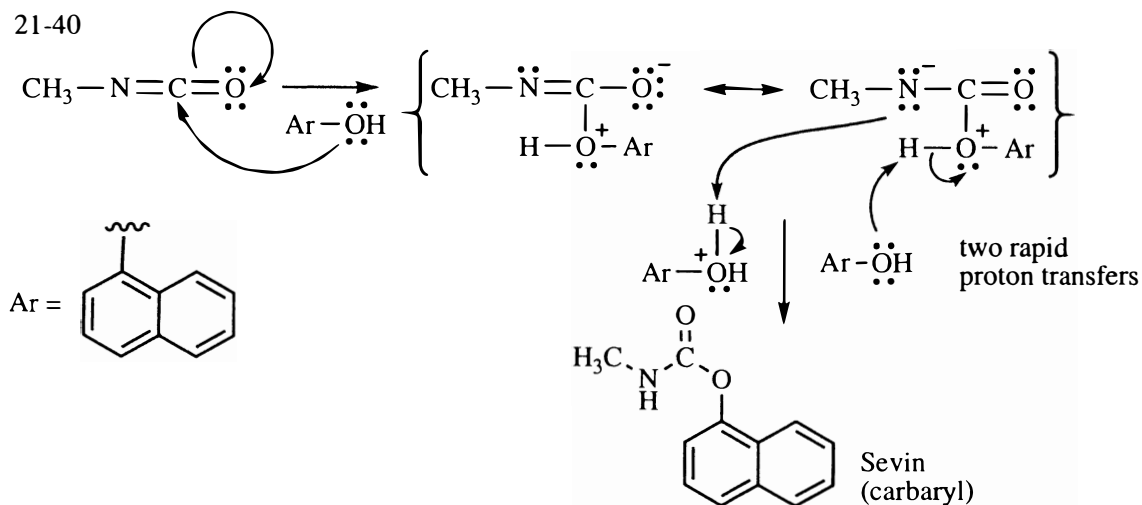
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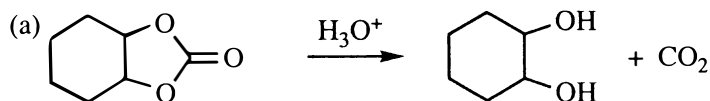
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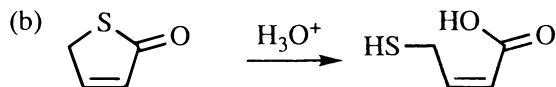
21-40



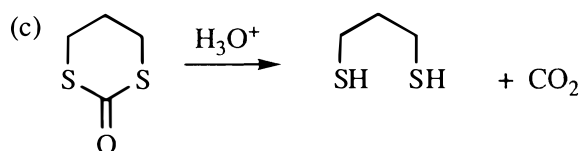
21-41



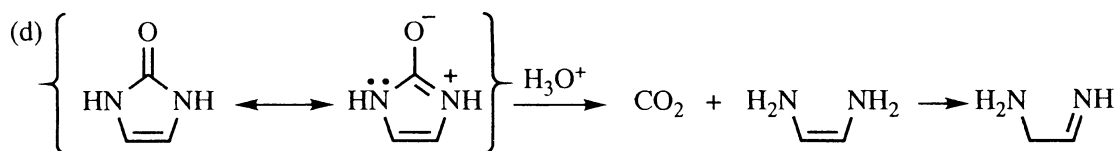
- (i) carbonate ester
(iii) not aromatic



- (i) thiolactone
(iii) not aromatic



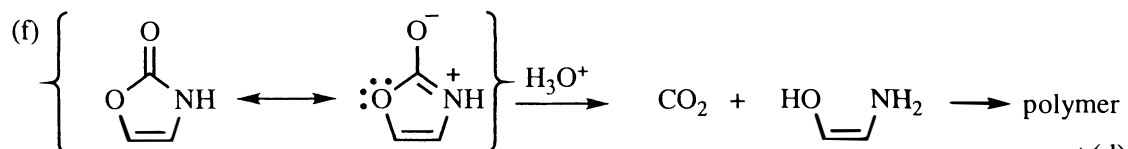
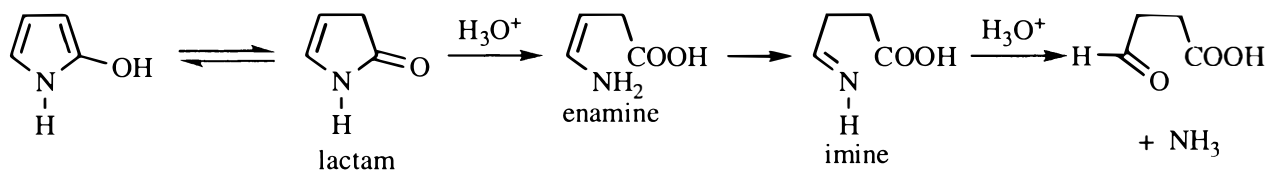
- (i) thiocarbonate ester
(iii) not aromatic



- (i) a substituted urea
(iii) AROMATIC—more easily seen in the resonance form shown

(The enediamine product would not be stable in aqueous acid. It would probably tautomerize to an imine, hydrolyze to ammonia and 2-aminoethanal, then polymerize.)

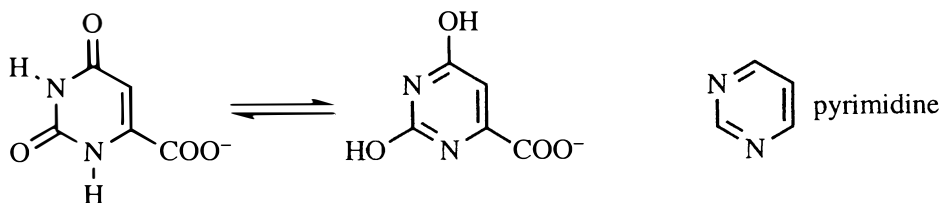
(e) At first glance, this AROMATIC compound does not appear to be an acid derivative. Like any enol, however, its tautomer must be considered.



- (i) a carbamate or urethane
(iii) AROMATIC—more easily seen in the resonance form

21-42

- (a) Carbamoyl phosphate is a mixed anhydride between carbamic acid and phosphoric acid. It would react easily with an amine to form an amide bond (technically, a urea), with phosphate as the leaving group.
 (b) N-Carbamoylaspartate has a carbonyl with two nitrogens on either side; this group is a urea derivative.
 (c) The NH_2 group on one end replaces the OH of a carboxylic acid on the other end; this reaction is a nucleophilic acyl substitution.
 (d) Orotate is aromatic as can be seen readily in the tautomer. It is called a "pyrimidine base" because of its structural similarity to the pyrimidine ring.

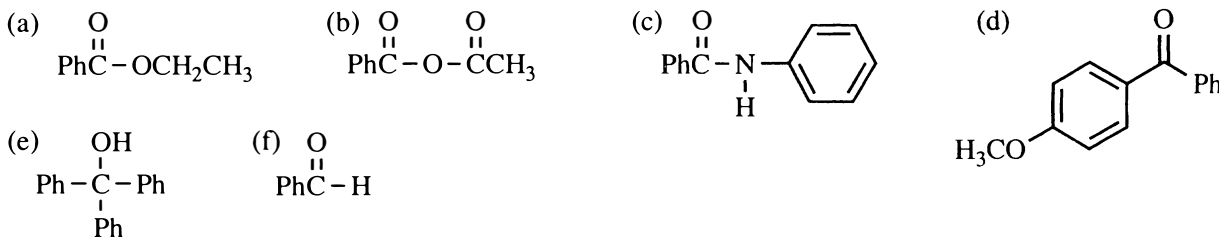


21-43 Please refer to solution 1-20, page 12 of this Solutions Manual.

21-44

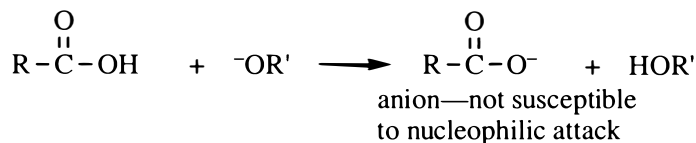
- (a) 3-methylpentanoyl chloride (g) benzonitrile
 (b) benzoic formic anhydride (h) 4-phenylbutane nitrile; γ -phenylbutyronitrile
 (c) acetanilide; *N*-phenylethanamide (i) dimethyl isophthalate, or dimethyl benzene-1,3-dicarboxylate
 (d) *N*-methylbenzamide (j) *N,N*-diethyl-3-methylbenzamide
 (e) phenyl acetate; phenyl ethanoate (k) 4-hydroxypentanoic acid lactone; γ -valerolactone
 (f) methyl benzoate (l) 3-aminopentanoic acid lactam; β -valerolactam

21-45

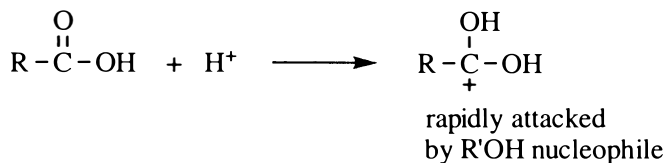


21-46 When a carboxylic acid is treated with a basic reagent, the base removes the acidic proton rather than attacking at the carbonyl (proton transfers are much faster than formation or cleavage of other types of bonds). Once the carboxylate anion is formed, the carbonyl is no longer susceptible to nucleophilic attack: nucleophiles do not attack sites of negative charge. By contrast, in acidic conditions, the protonated carbonyl has a positive charge and is activated to nucleophilic attack.

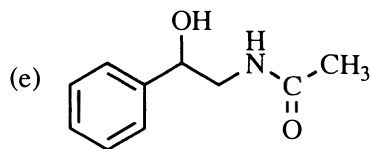
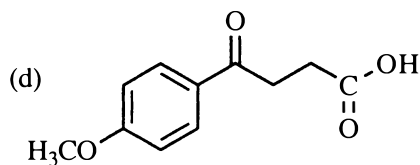
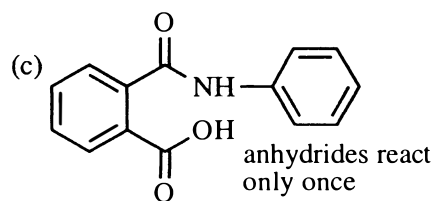
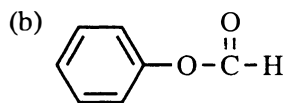
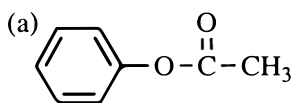
basic conditions



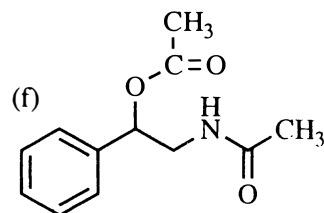
acidic conditions



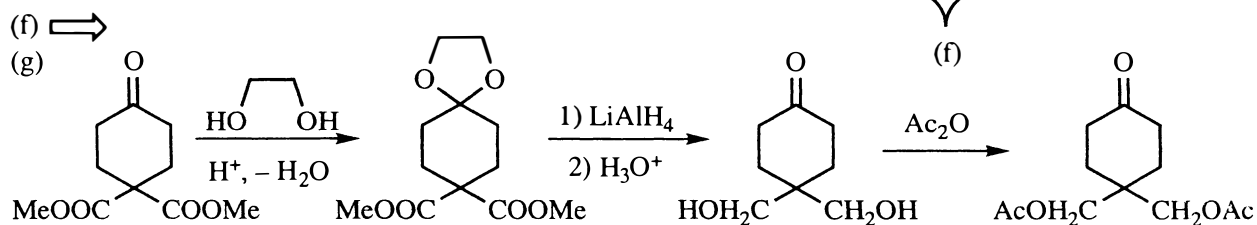
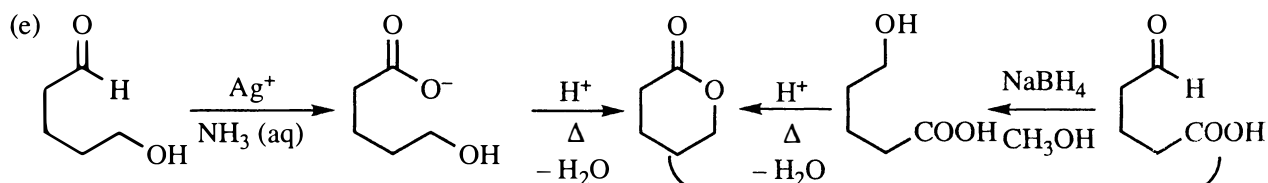
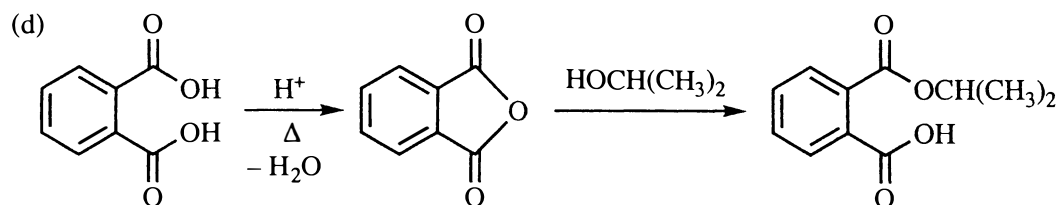
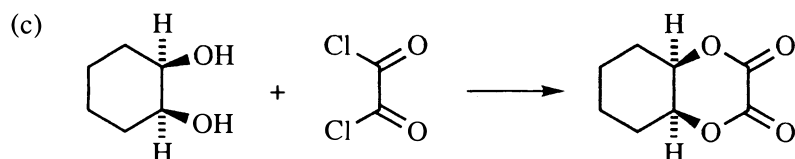
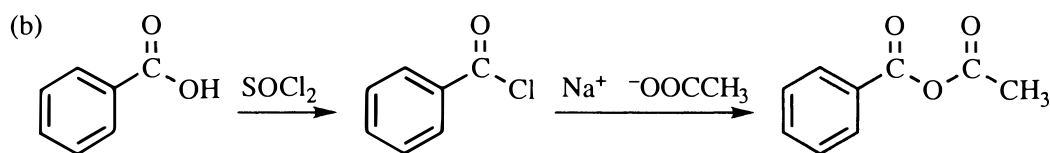
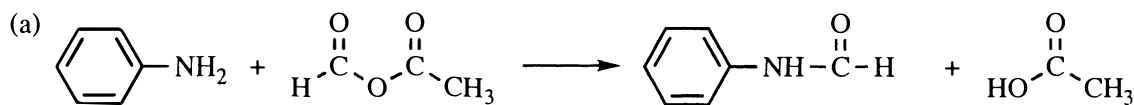
21-47



amines are more nucleophilic than alcohols

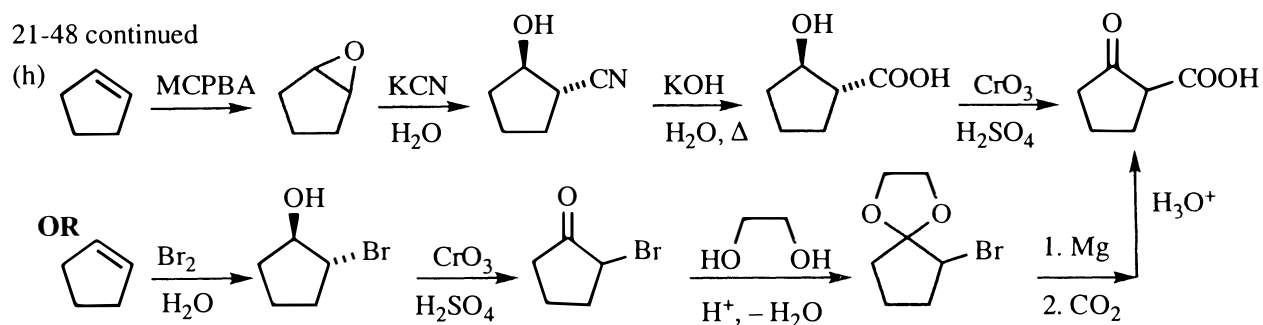


21-48

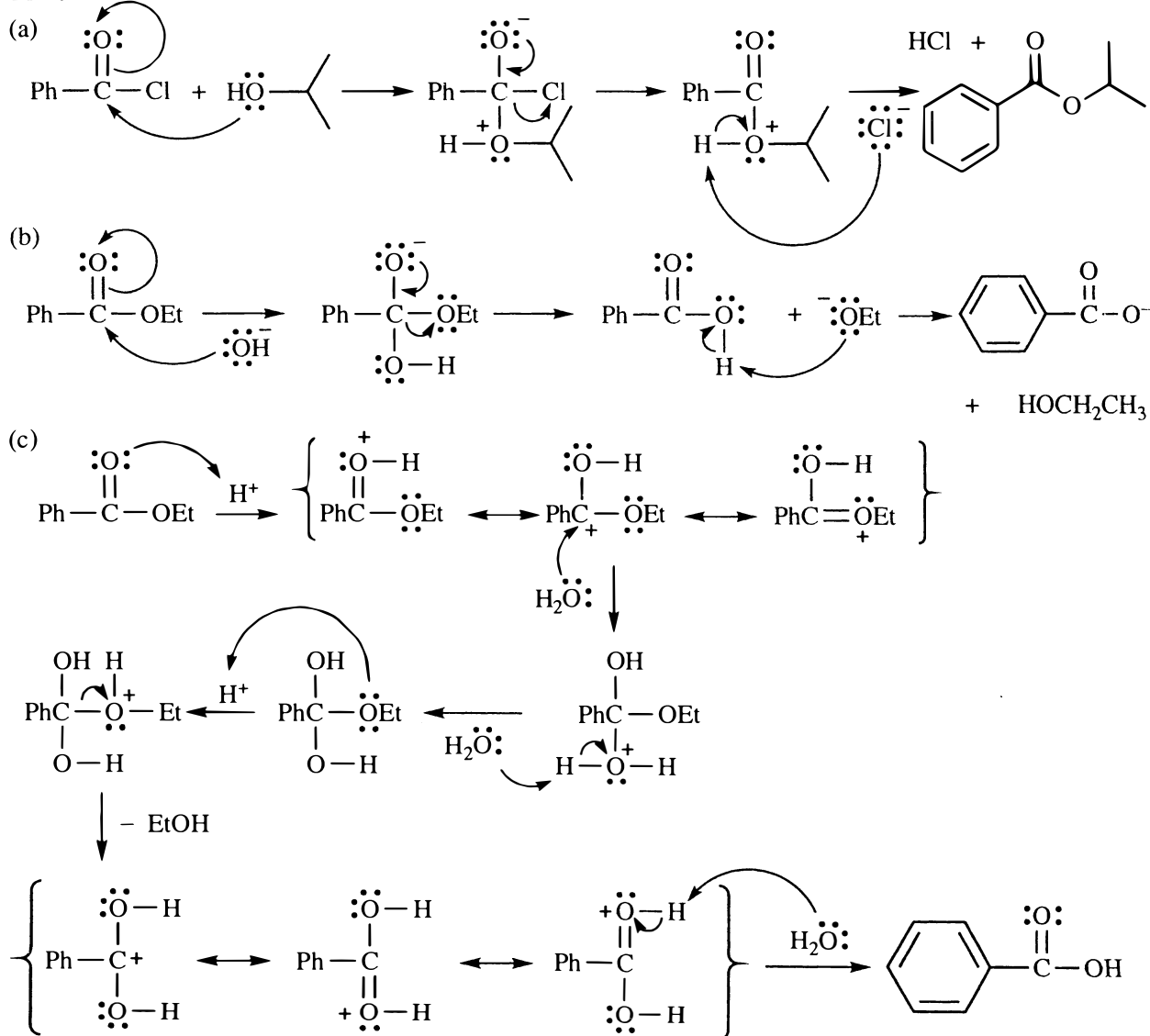
any ester where ethylene glycol displaces methanol will be reduced with LiAlH₄

aqueous acid workup removes ketal protecting group

21-48 continued

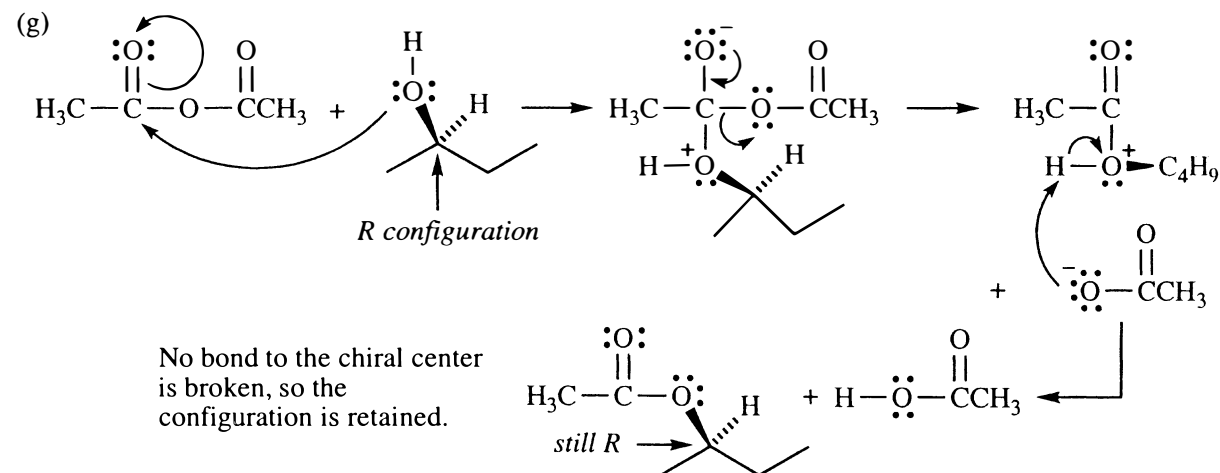
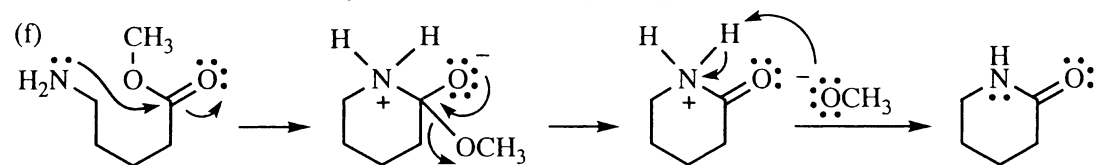
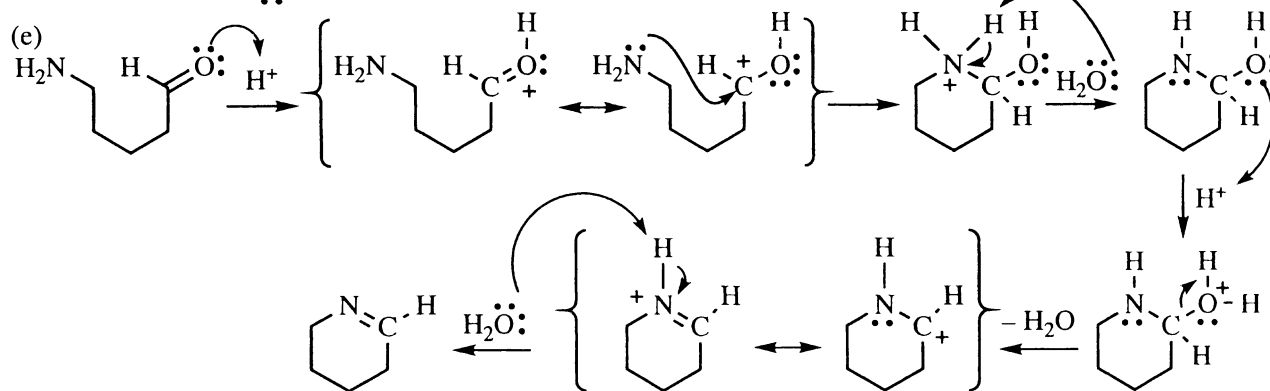
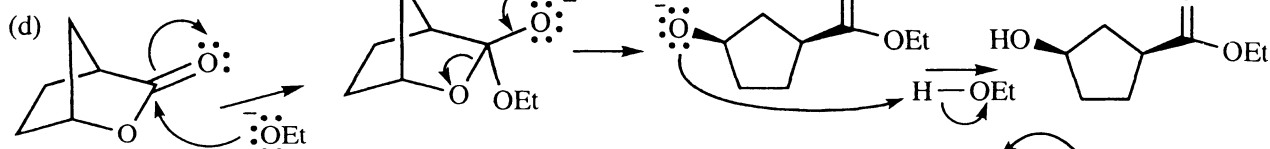


21-49

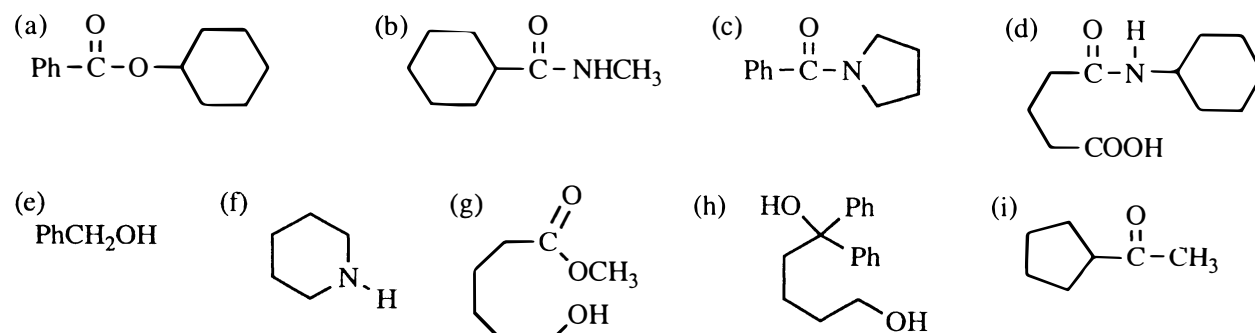


Note: species with positive charge on carbon adjacent to benzene also have resonance forms (not shown) with the positive charge distributed over the ring.

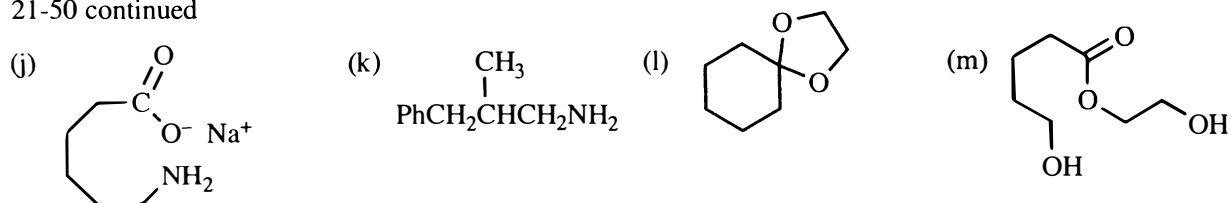
21-49 continued



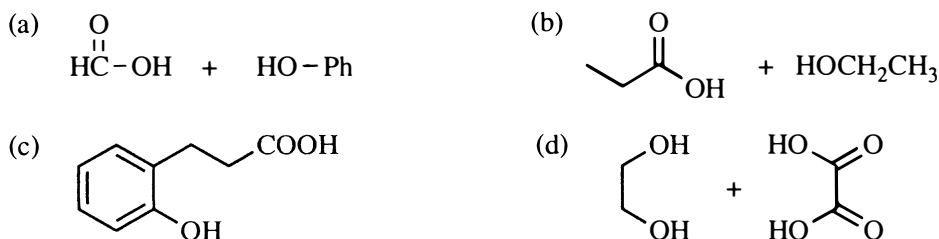
21-50



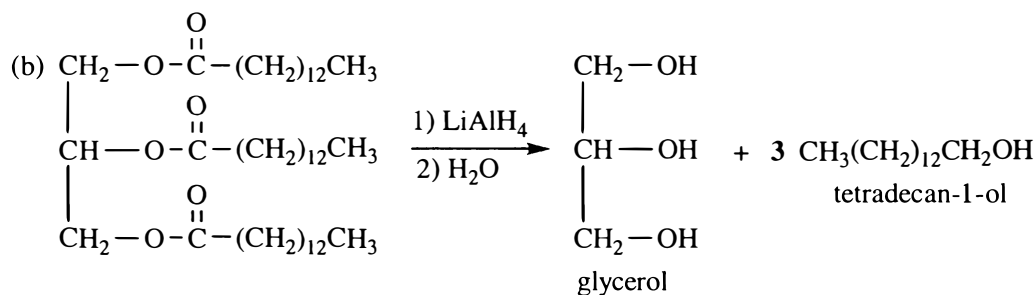
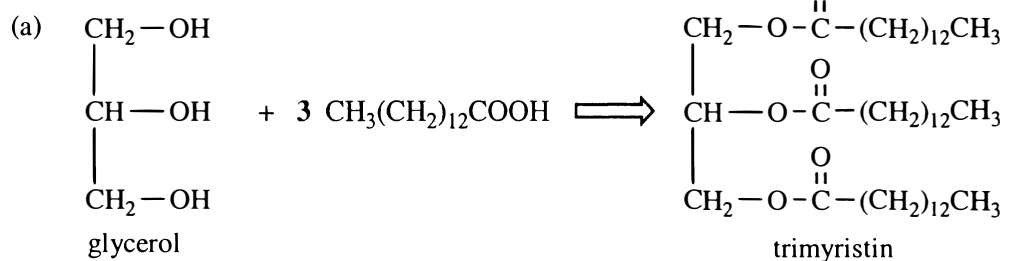
21-50 continued



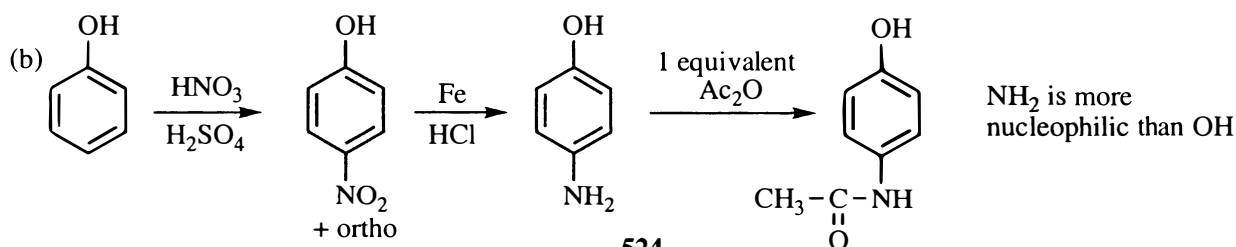
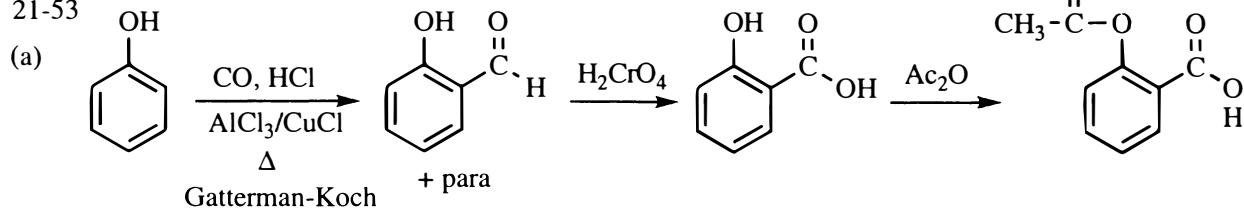
21-51 Products after adding dilute acid in the workup:



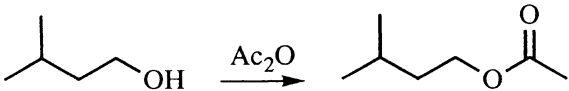
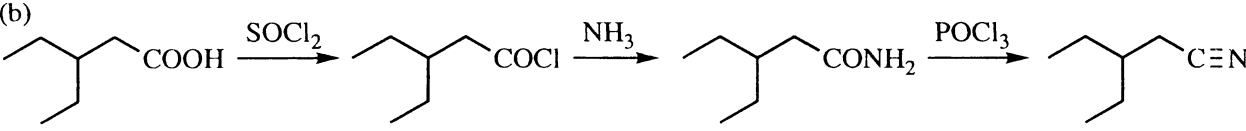
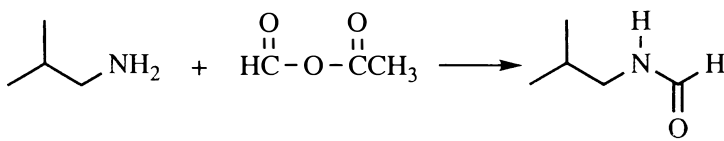
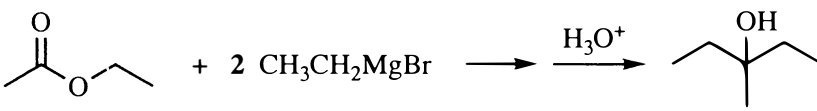
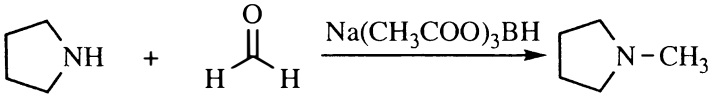
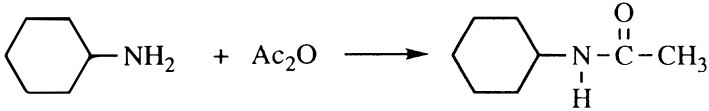
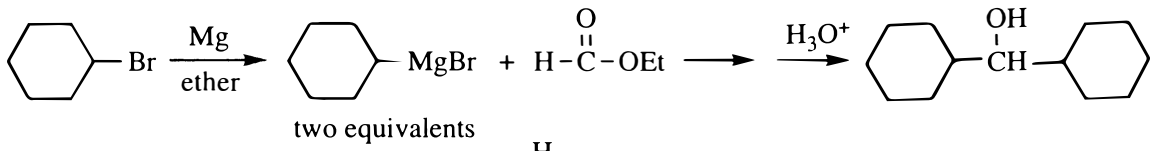
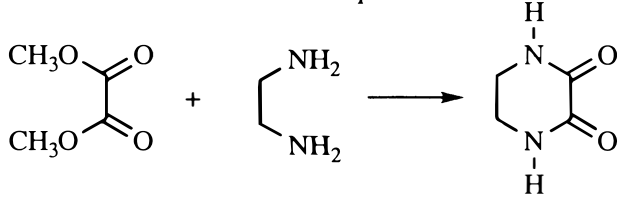
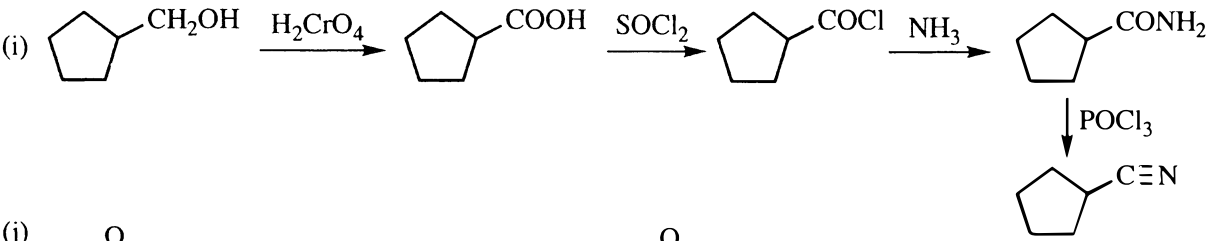
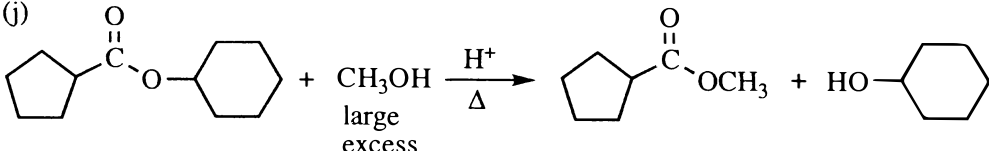
21-52



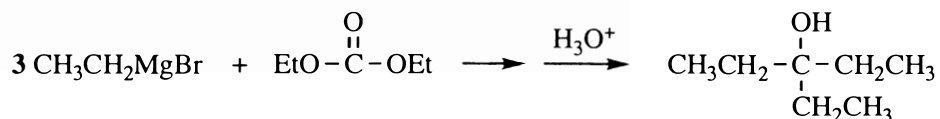
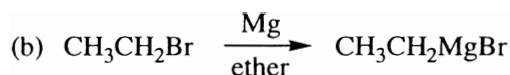
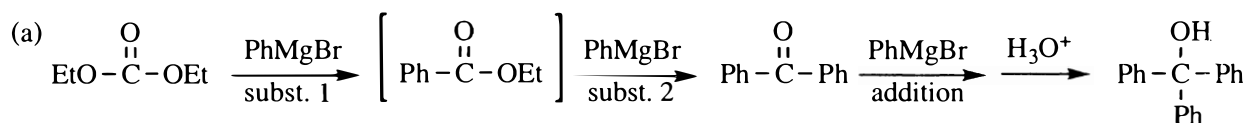
21-53



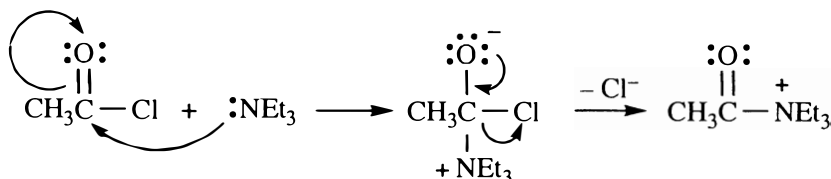
21-54

- (a) 
- (b) 
- (c) 
- (d) 
- (e) See the solution to 21.36(b) for one method. Here is another: reductive alkylation.
- 
- (f) 
- (g) 
- (h) 
- (i) 
- (j) 

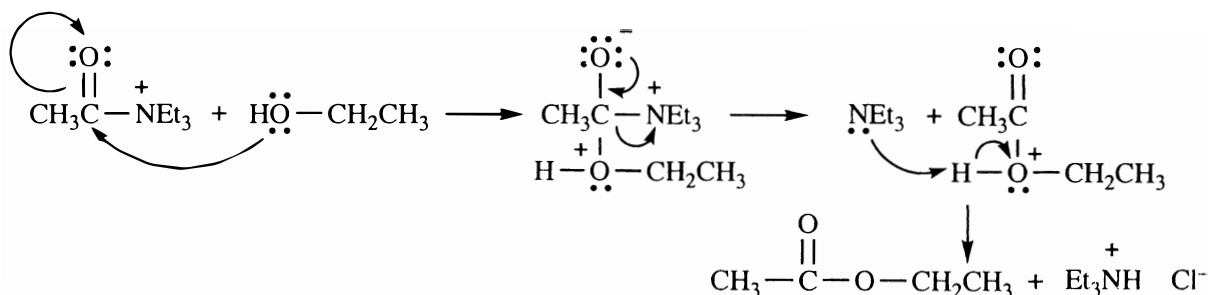
21-55 Diethyl carbonate has *two* leaving groups on the carbonyl. It can undergo *two* nucleophilic acyl substitutions, followed by one nucleophilic addition.



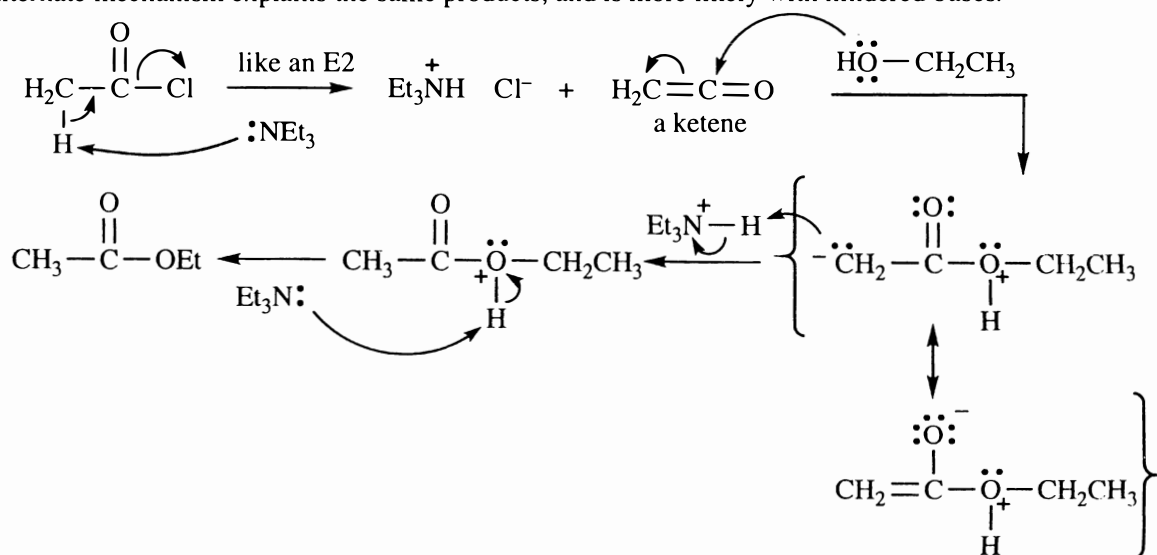
21-56 Triethylamine is nucleophilic, but it has no H on nitrogen to lose, so it forms a salt instead of a stable amide.



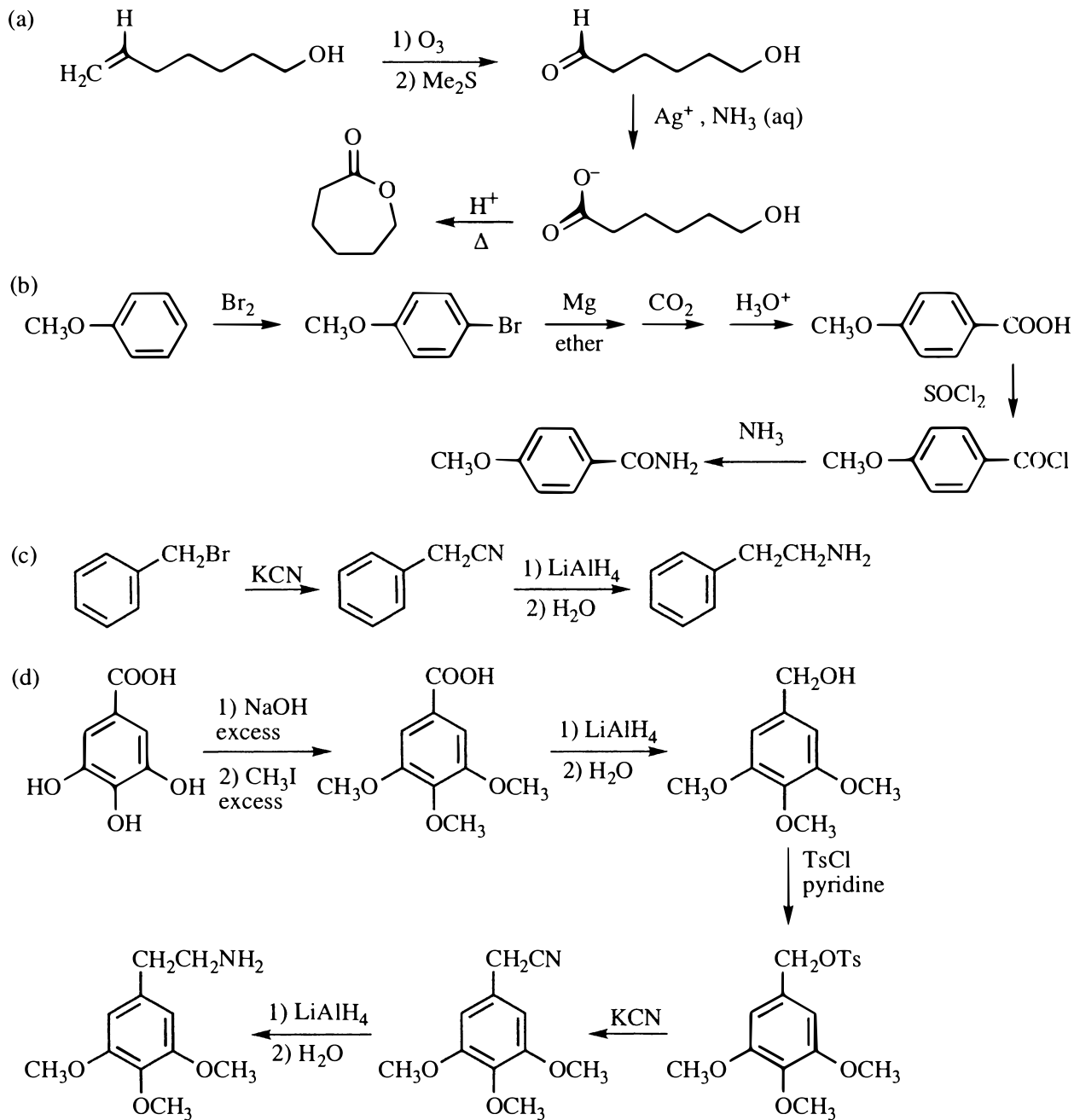
When ethanol is added, it attacks the carbonyl of the salt, with triethylamine as the leaving group.

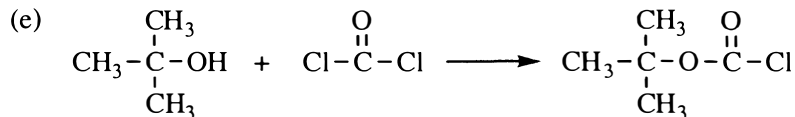
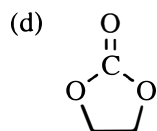
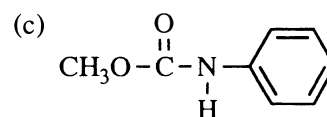
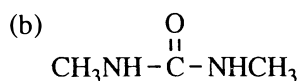
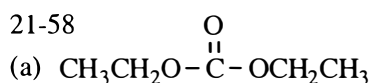


An alternate mechanism explains the same products, and is more likely with hindered bases:



21-57





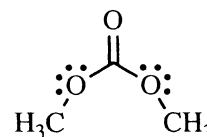
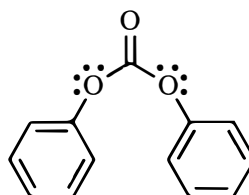
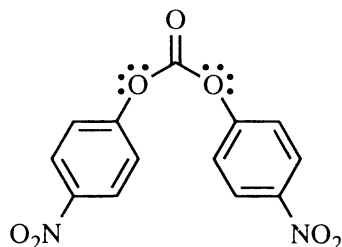
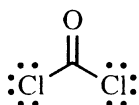
21-59 (a) The rate of these nucleophilic acyl substitution reactions is controlled by two factors: stability of the starting material as determined by the amount of resonance donation from the leaving group into the carbonyl, and the leaving group ability which is determined by the basicity of the leaving group, the least basic being the best leaving group.

LEAST STABLE: no significant sharing of electrons from chlorine

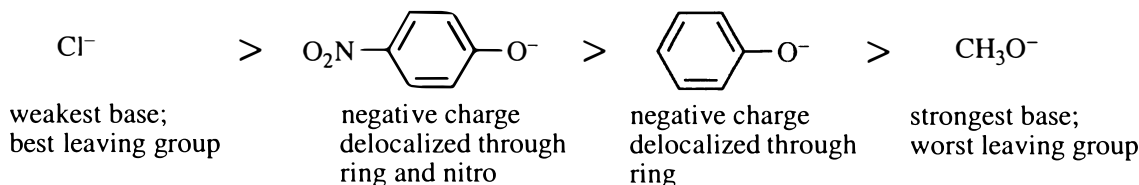
electrons from oxygen are also distributed through the ring and nitro; very little resonance stabilization

electrons from oxygen are also distributed through the ring; small resonance stabilization

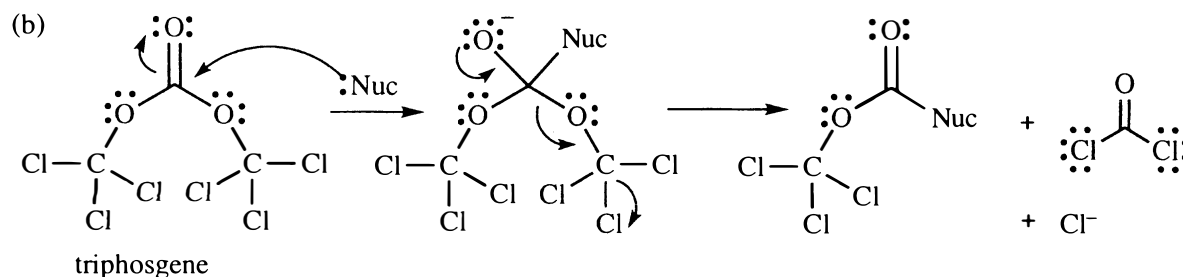
MOST STABLE: most significant resonance donation of electrons from oxygen



leaving group ability and basicity:

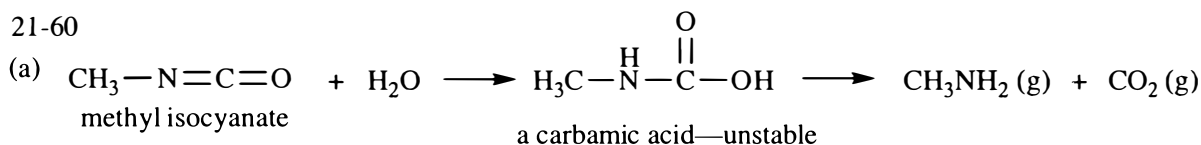


The least stable starting material with the best leaving group will be fastest to react. The most stable starting material with the poorest leaving group will be slowest to react.

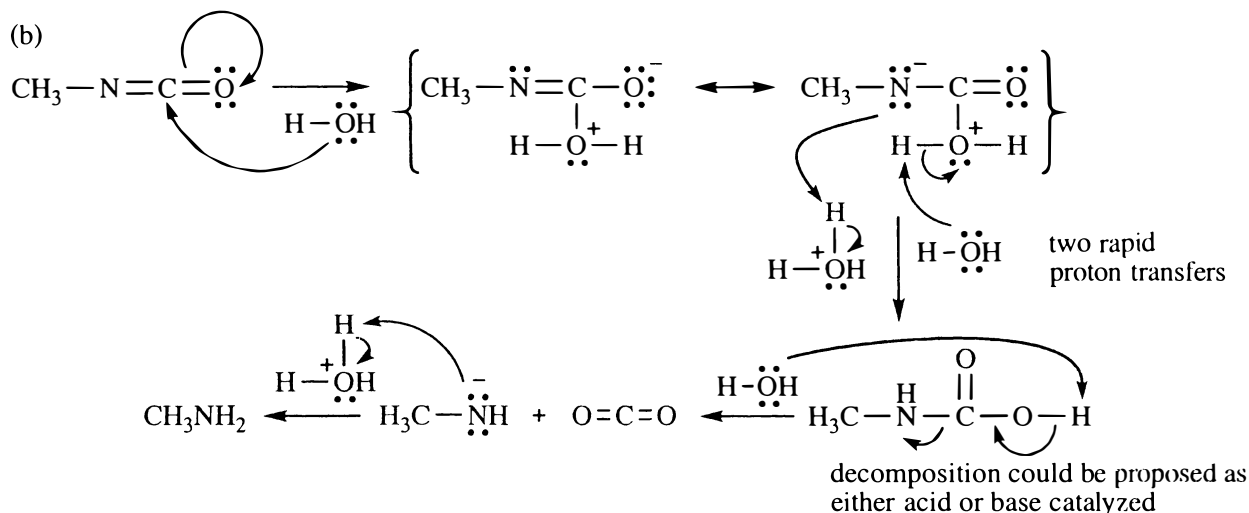


The first step is the standard attack of a nucleophile like CH_3OH at the carbonyl carbon to make the tetrahedral intermediate. The second step is key: the collapse of the tetrahedral intermediate produces one equivalent of phosgene. Attack of a second nucleophile of the other side of triphosgene would release a latent (hidden or trapped) equivalent of phosgene from that side too. Thus, the equivalent of three molecules of phosgene are locked into the triphosgene molecule. Eventually, all six positions would be substituted with methanol producing three molecules of dimethyl carbonate for each molecule of triphosgene.

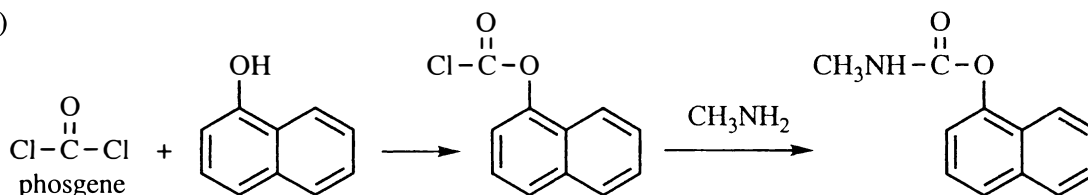
21-60



Both of these reactions are exothermic. In a closed vessel like an industrial reactor, the production of gaseous products causes a large pressure increase, risking an explosion.



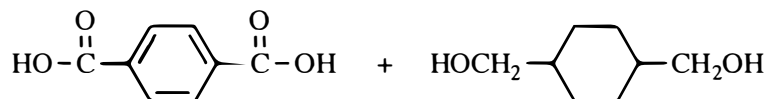
(c)



21-61

(a) (i) The repeating functional group is an ester, so the polymer is a polyester (named Kodel®).

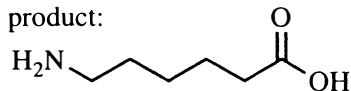
(ii) hydrolysis products:



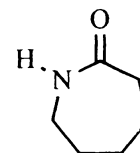
(iii) The monomers could be the same as the hydrolysis products, or else some reactive derivative of the dicarboxylic acid, like an acid chloride or an ester derivative.

(b) (i) The repeating functional group is an amide, so the polymer is a polyamide (named Nylon 6).

(ii) hydrolysis product:

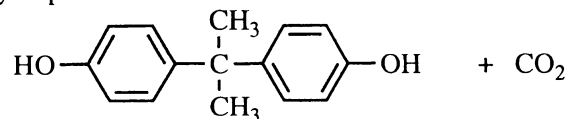


(iii) The monomer could be the same as the hydrolysis product, but in the polymer industry, the actual monomer used is the lactam shown at the right.



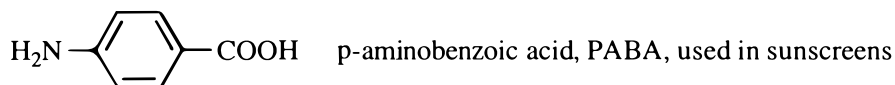
21-61 continued

- (c) (i) The repeating functional group is a carbonate, so the polymer is a polycarbonate (named Lexan®).
 (ii) hydrolysis products:



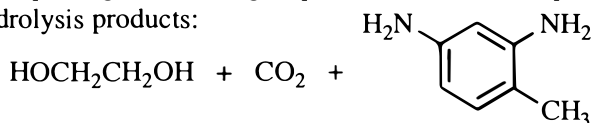
(iii) The phenol monomer would be the same as the hydrolysis product; phosgene or a carbonate ester would be the other monomer.

- (d) (i) The repeating functional group is an amide, so the polymer is a polyamide.
 (ii) hydrolysis product:

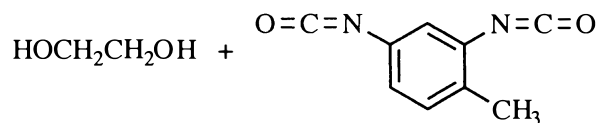


(iii) The monomer could be the same as the hydrolysis product; a reactive derivative of the acid like an ester could also be used.

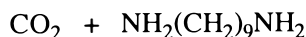
- (e) (i) The repeating functional group is a urethane, so the polymer is a polyurethane.
 (ii) hydrolysis products:



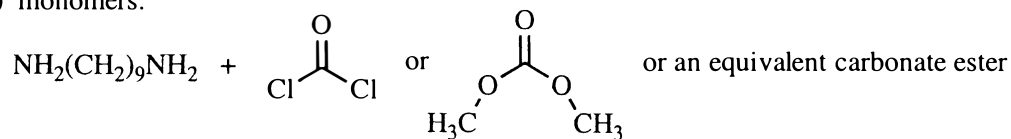
(iii) monomers:



- (f) (i) The repeating functional group is a urea, so the polymer is a polyurea.
 (ii) hydrolysis products:



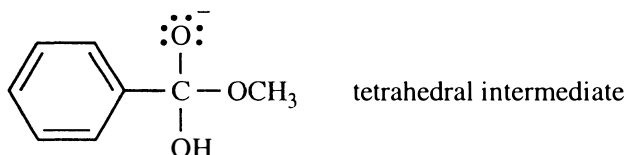
(iii) monomers:



21-62

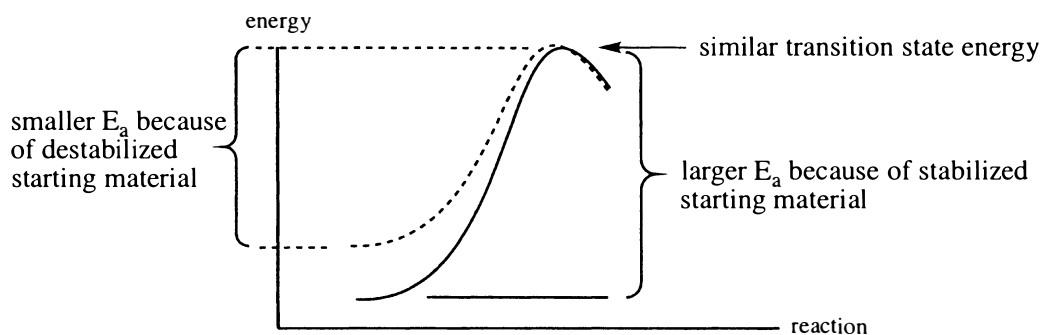
- (a) Both structures are β -lactam antibiotics, a penicillin and a cephalosporin.
 (b) "Cephalosporin N" has a 5-membered, sulfur-containing ring. This belongs in the penicillin class of antibiotics.

21-63 The rate of a reaction depends on its activation energy, that is, the difference in energy between starting material and the transition state. The transition state in saponification is similar in structure, and therefore in energy, to the tetrahedral intermediate:

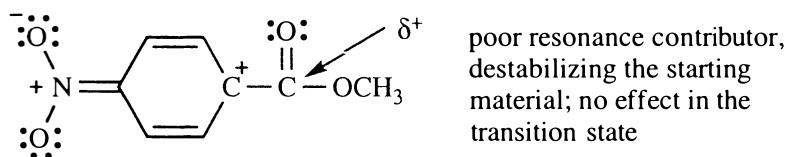


The tetrahedral carbon has no resonance overlap with the benzene ring, so any resonance effect of a substituent on the ring will have very little influence on the energy of the transition state.

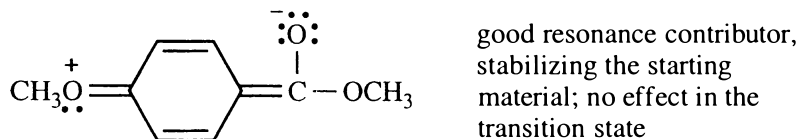
What will have a big influence on the activation energy is whether a substituent stabilizes or destabilizes the starting material. Anything that stabilizes the starting material will therefore increase the activation energy, slowing the reaction; anything that destabilizes the starting material will decrease the activation energy, speeding the reaction.



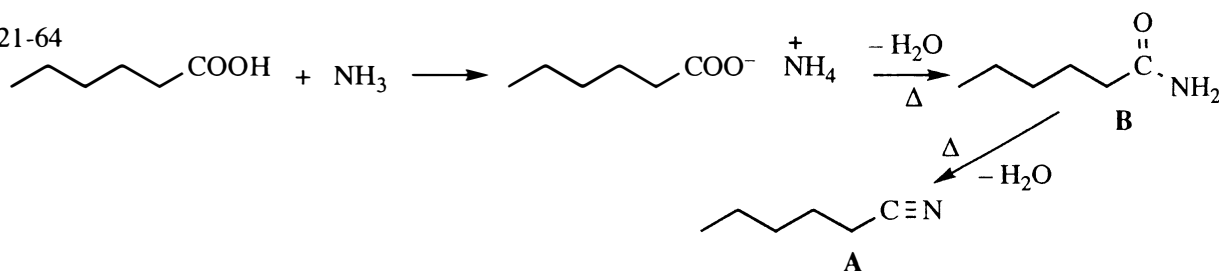
(a) One of the resonance forms of methyl *p*-nitrobenzoate has a positive charge on the benzene carbon adjacent to the positive carbonyl carbon. This resonance form destabilizes the starting material, lowering the activation energy, speeding the reaction.



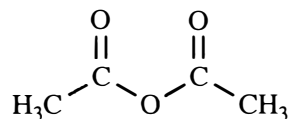
(b) One of the resonance forms of methyl *p*-methoxybenzoate has all atoms with full octets, and negative charge on the most electronegative atom. This resonance form stabilizes the starting material, increasing the activation energy, slowing the reaction.



21-64



21-65 A singlet at δ 2.15 is H on carbon next to carbonyl, the only type of proton in the compound. The IR spectrum shows no OH, and shows two carbonyl absorptions at high frequency, characteristic of an anhydride. Mass of the molecular ion at 102 proves that the anhydride must be acetic anhydride, a reagent commonly used in aspirin synthesis.



Acetic anhydride can be disposed of by hydrolyzing (carefully! exothermic!) and neutralizing in aqueous base.

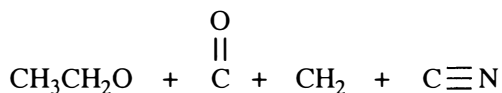
21-66

IR spectrum:

—sharp spike at $2250\text{ cm}^{-1} \Rightarrow \text{C}\equiv\text{N}$
 — $1750\text{ cm}^{-1} \Rightarrow \text{C}=\text{O}$
 — $1200\text{ cm}^{-1} \Rightarrow \text{C}-\text{O}$ } maybe an ester

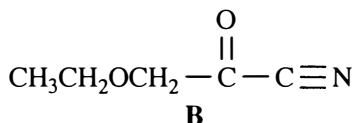
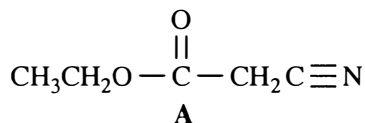
NMR spectrum:

—triplet and quartet $\Rightarrow \text{CH}_3\text{CH}_2$
 —this quartet at δ 4.3 $\Rightarrow \text{CH}_3\text{CH}_2\text{O}$
 —2H singlet at δ 3.5 $\Rightarrow$ isolated CH_2



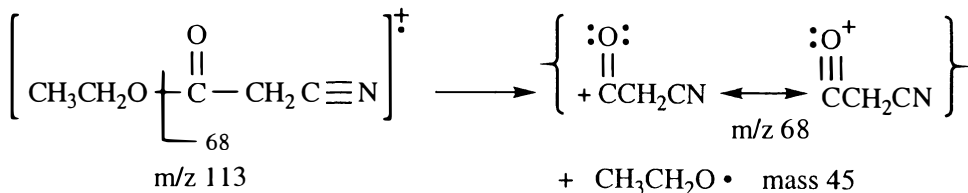
sum of the masses is 113, consistent with the MS

The fragments can be combined in only two possible ways:



The NMR proves the structure to be **A**. If the structure were **B**, the CH_2 between oxygen and the carbonyl would come farther downfield than the CH_2 of the ethyl (deshielded by oxygen and carbonyl instead of by oxygen alone). As this is not the case, the structure cannot be **B**.

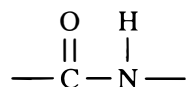
The peak in the mass spectrum at m/z 68 is due to α -cleavage of the ester:



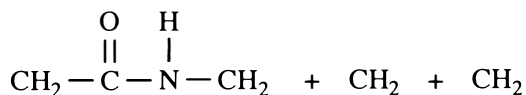
21-67

The formula C_5H_9NO has 2 elements of unsaturation.

IR spectrum: The strongest peak at 1670 cm^{-1} comes low in the carbonyl region; in the absence of conjugation (no alkene peak observed), a carbonyl this low is almost certainly an amide. There is one broad peak in the NH/OH region, hinting at the likelihood of a secondary amide.

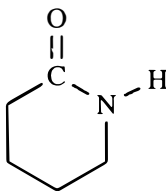


HNMR spectrum: The broad peak at $\delta 7.55$ is exchangeable with D_2O ; this is an amide proton. A broad, 2H peak at $\delta 3.3$ is a CH_2 next to nitrogen. A broad, 2H peak at $\delta 2.4$ is a CH_2 next to carbonyl. The 4H peak at $\delta 1.8$ is probably two more CH_2 groups. There appears to be coupling among these protons but it is not resolved enough to be useful for interpretation. This is often the case when the compound is cyclic, with restricted rotation around carbon-carbon bonds, giving *non-equivalent* (axial and equatorial) hydrogens on the same carbon.



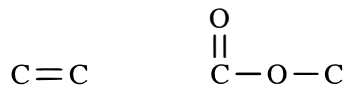
CNMR spectrum: The peak at $\delta 175$ is the $C=O$ of the amide. All of the peaks between $\delta 25$ and $\delta 50$ are aliphatic sp^3 carbons, no sp^2 carbons, so the remaining element of unsaturation cannot be a $C=C$; it must be a ring. The carbon peak farthest downfield is the carbon adjacent to N.

The most consistent structure:

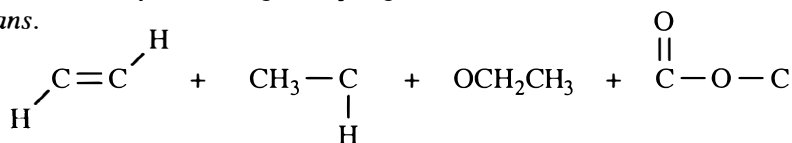


δ -valerolactam

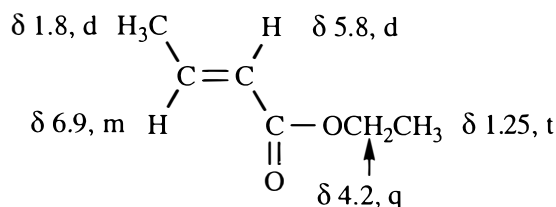
IR spectrum: A strong carbonyl peak at 1720 cm^{-1} , in conjunction with the C—O peak at 1200 cm^{-1} , suggests the presence of an ester. An alkene peak appears at 1660 cm^{-1} .



HNMR spectrum: The typical ethyl pattern stands out: 3H triplet at δ 1.25 and 2H quartet at δ 4.2. The chemical shift of the CH_2 suggests it is bonded to an oxygen. The other groups are: a 3H doublet at δ 1.8, likely to be a CH_3 next to one H; a 1H doublet at δ 5.8, a vinyl hydrogen with one neighboring H; and a 1H multiplet at δ 6.9, another vinyl H with many neighbors, the far downfield chemical shift suggesting that it is beta to the carbonyl. The large coupling constant in the doublet at δ 5.8 shows that the two vinyl hydrogens are *trans*.



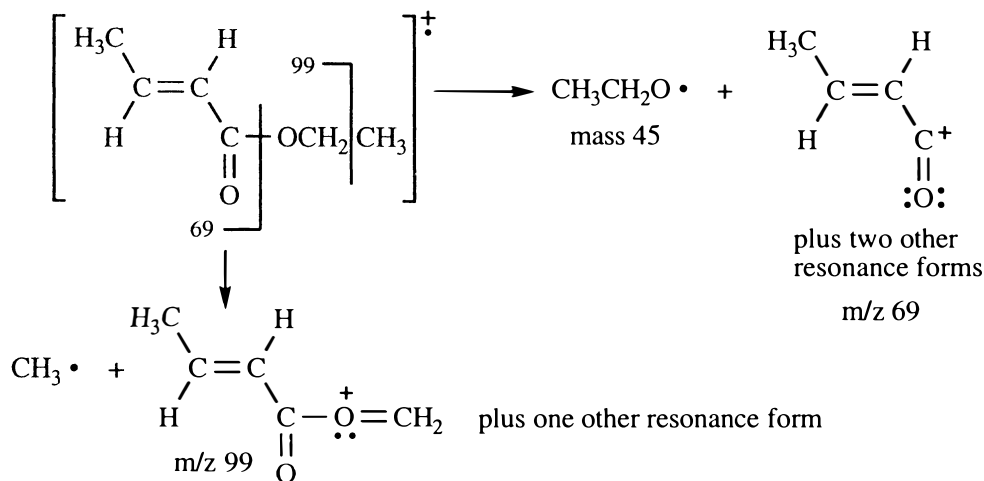
There is only one possible way to assemble these pieces:



CNMR spectrum: The six unique carbons are unmistakable: the $\text{C}=\text{O}$ of the ester at δ 166; the two vinyl carbons at δ 144 (beta to $\text{C}=\text{O}$) and at δ 123 (alpha to $\text{C}=\text{O}$); the CH_2-O of the ester at δ 60; and the two methyls at δ 18 and at δ 14.

Mass spectrum: This structure has mass 114, consistent with the molecular ion.

Major fragmentations:



21-69 If you solved this problem, put a gold star on your forehead.

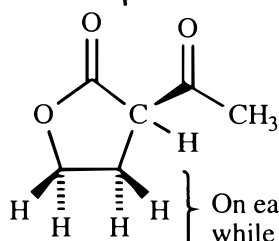
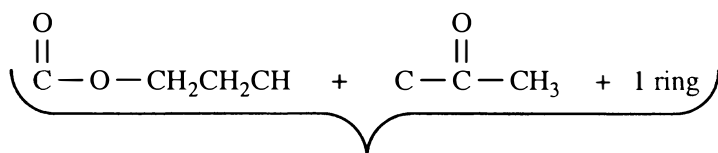
The formula $C_6H_8O_3$ indicates 3 elements of unsaturation.

IR spectrum: The absence of strong OH peaks shows that the compound is neither an alcohol nor a carboxylic acid. There are two carbonyl absorptions: the one about 1770 cm^{-1} is likely a strained cyclic ester (reinforced with the C—O peak around 1150 cm^{-1}), while the one at 1720 cm^{-1} is probably a ketone. (An anhydride also has two peaks, but they are of higher frequency than the ones in this spectrum.)



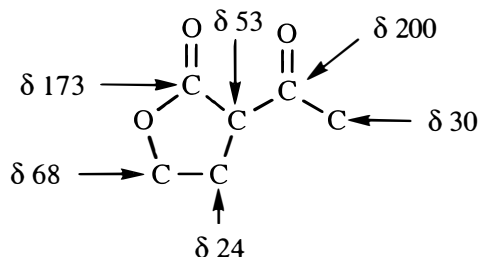
Proton NMR spectrum: The NMR shows four types of protons. The 2H triplet at δ 4.3 is a CH_2 group next to an oxygen on one side, with a CH_2 on the other. The 1H multiplet at δ 3.7 is also strongly deshielded (probably by two carbonyls), a CH next to a CH_2 . The 3H singlet at δ 2.45 is a CH_3 on one of the carbonyls. The remaining two hydrogens are highly coupled, a CH_2 where the two hydrogens are not equivalent. There are no vinyl hydrogens (and no alkene carbon in the carbon NMR), so the remaining element of unsaturation must be a ring.

Assemble the pieces:



On each carbon, the "up" hydrogen is cis to the acetyl group, while the "down" hydrogen is trans. Thus, the two hydrogens on each of these carbons are not equivalent, leading to complex splitting.

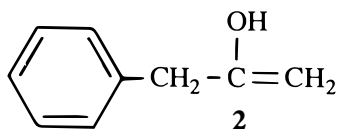
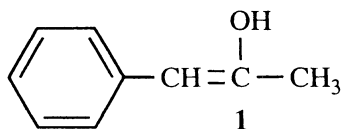
Carbon NMR:



CHAPTER 22—
CONDENSATIONS AND ALPHA SUBSTITUTIONS OF CARBONYL COMPOUNDS

22-1

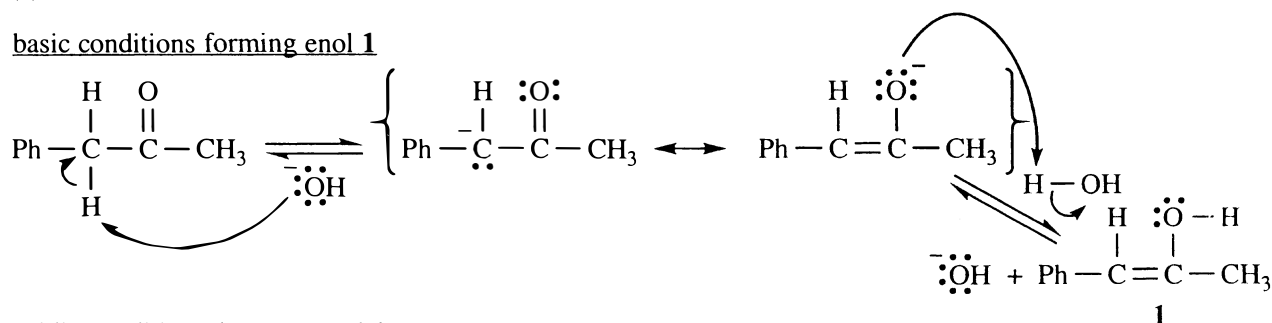
(a)



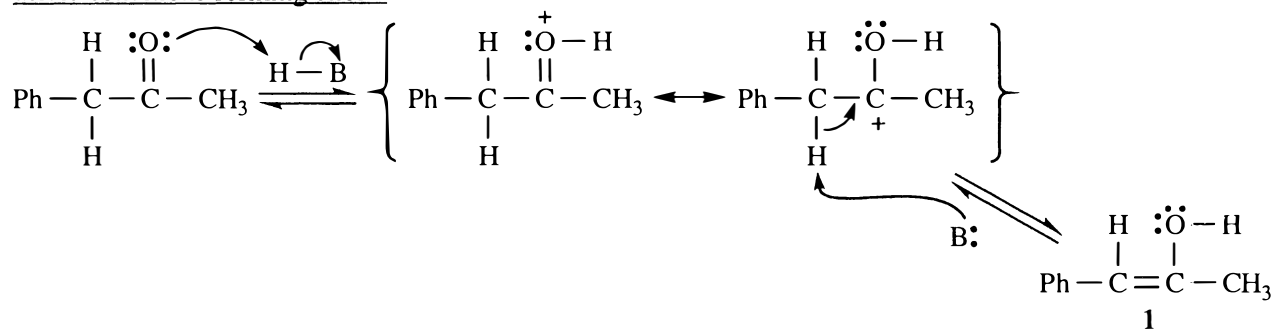
(b) Enol **1** will predominate at equilibrium as its double bond is conjugated with the benzene ring, making it more stable than **2**.

(c)

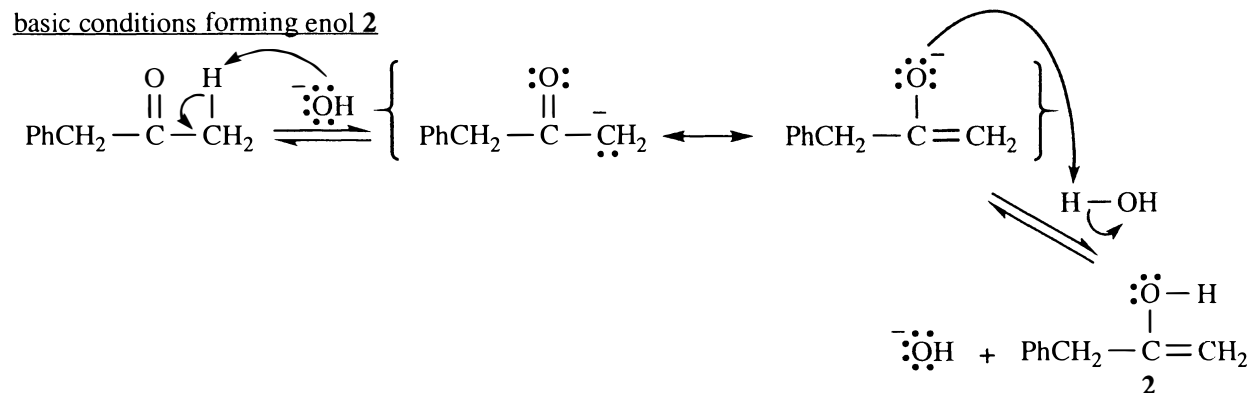
basic conditions forming enol **1**



acidic conditions forming enol **1**

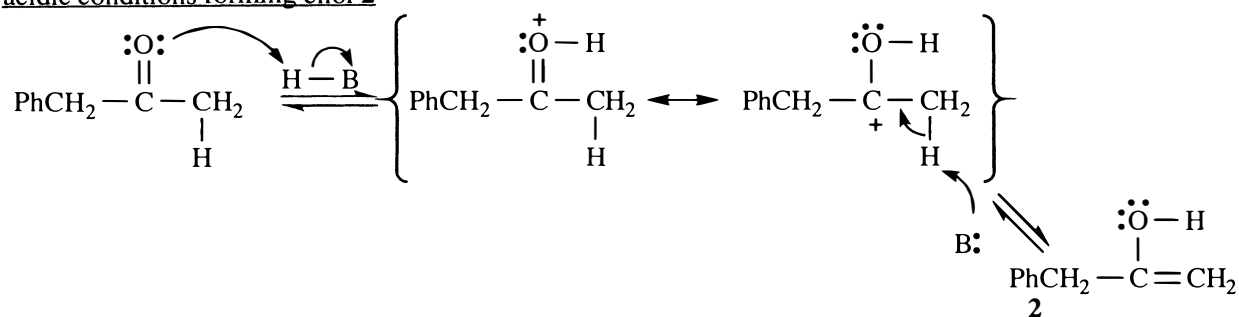


basic conditions forming enol **2**

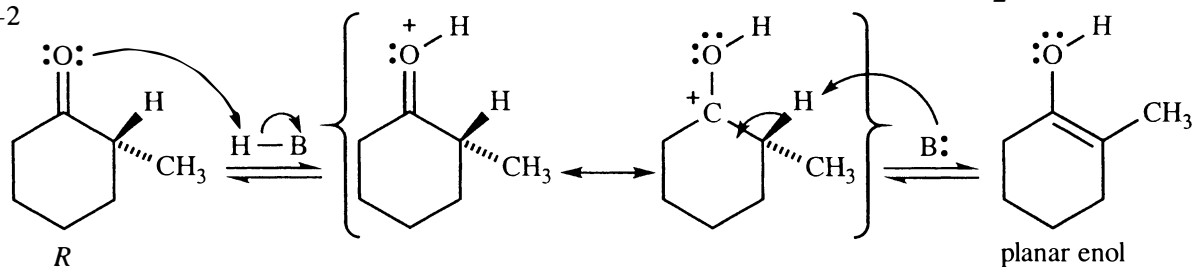


22-1 (c) continued

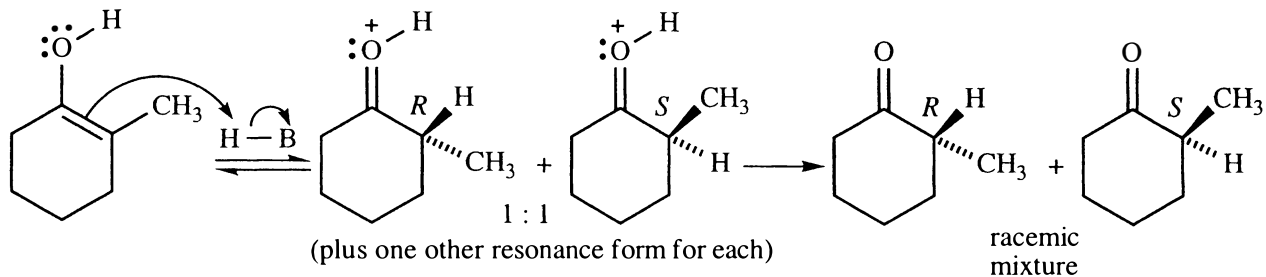
acidic conditions forming enol 2



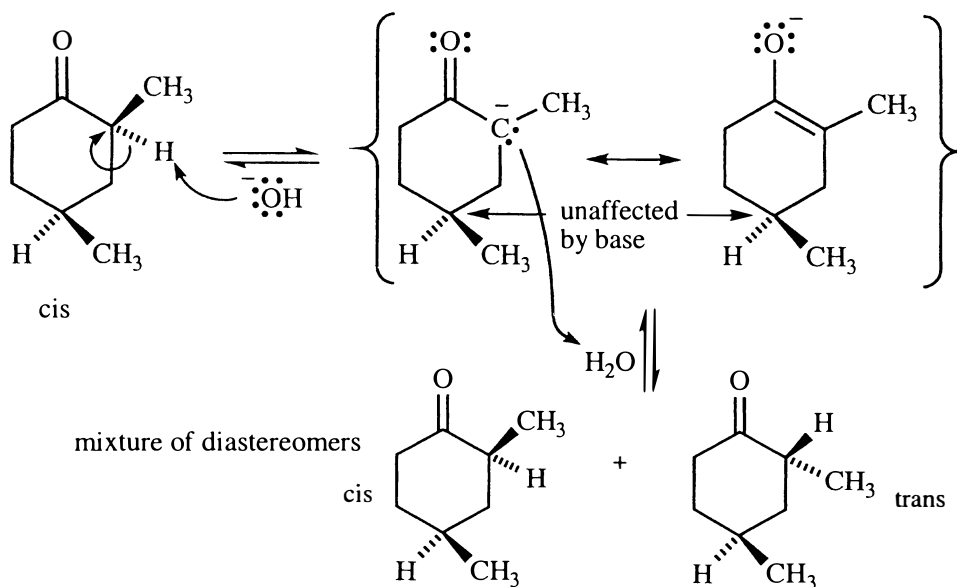
22-2



This planar enol intermediate has lost all chirality. Protonation can occur with equal probability at either face of the pi bond leading to racemic product.

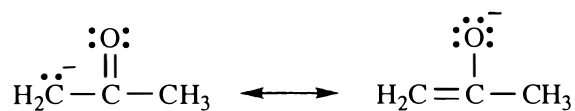


22-3

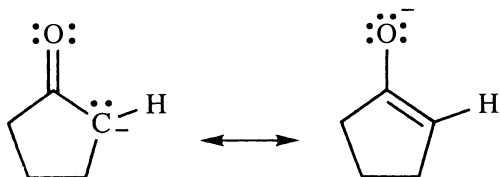


22-4

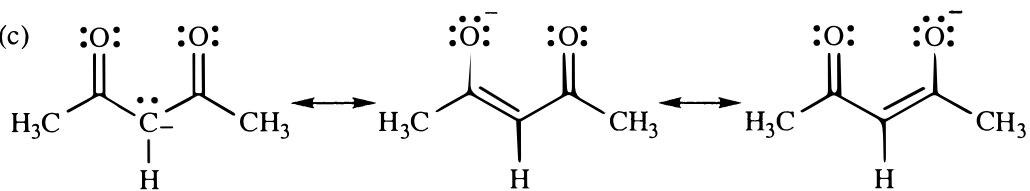
(a)



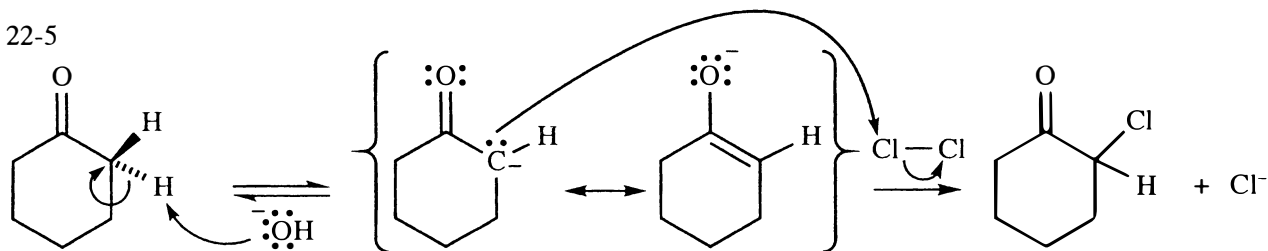
(b)



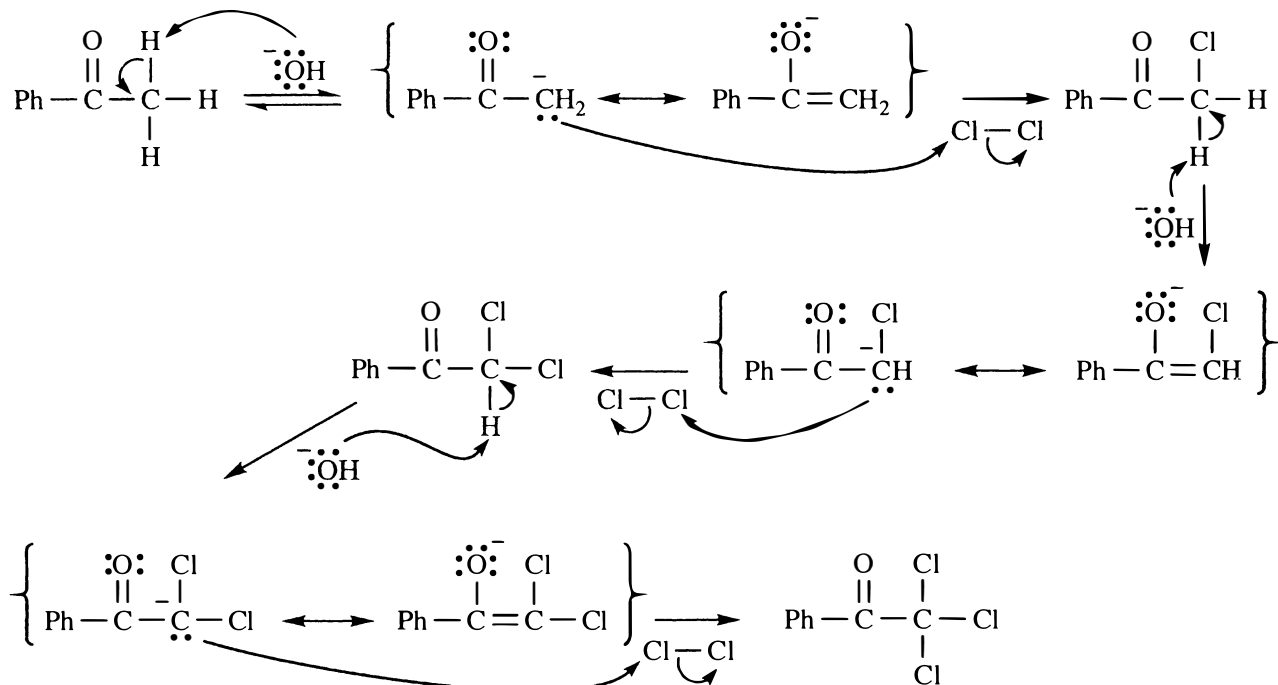
(c)



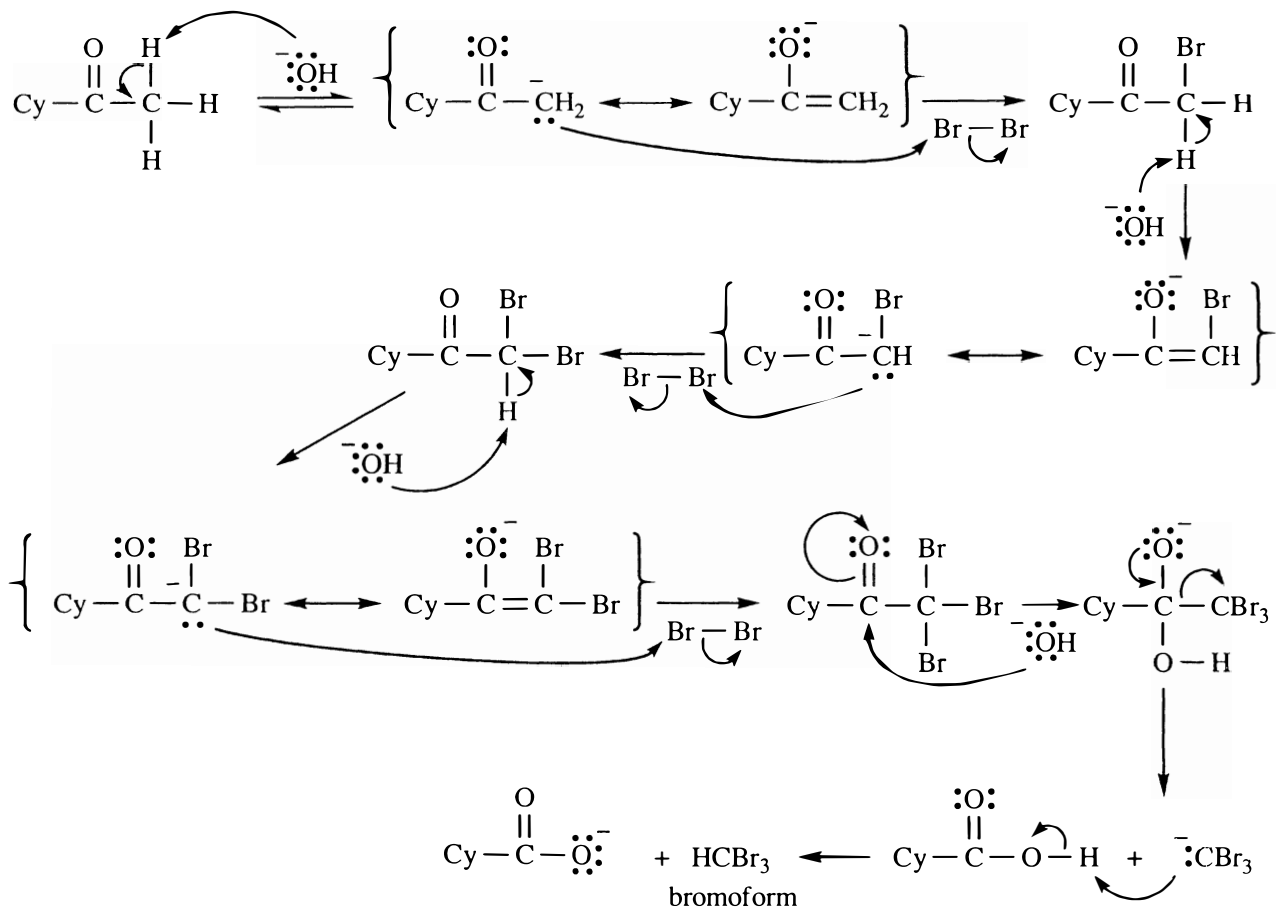
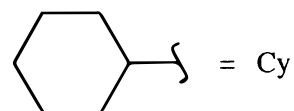
22-5



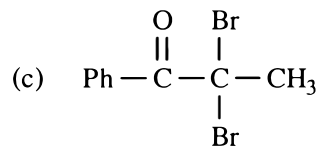
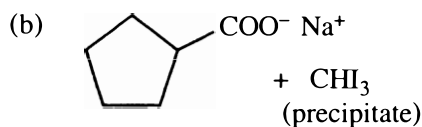
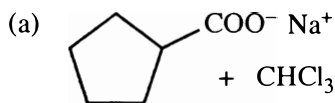
22-6



22-7 For this problem, the cyclohexyl group is abbreviated "Cy".

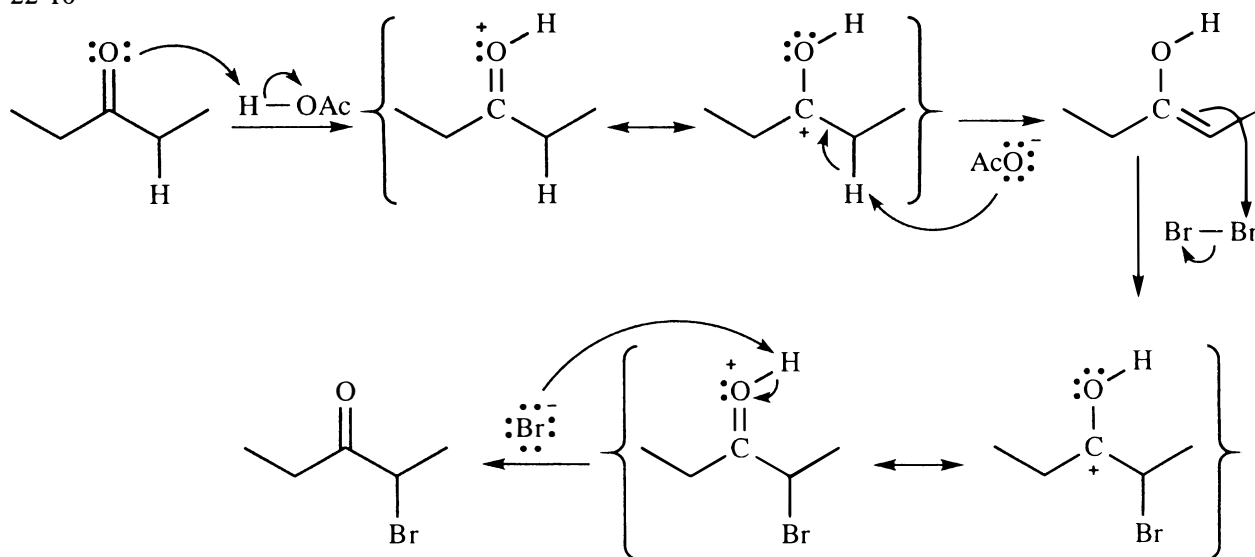


22-8

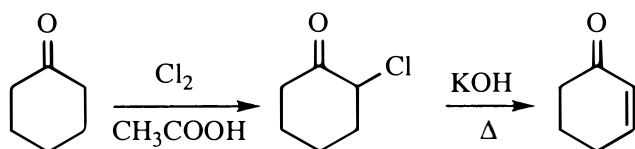


22-9 Methyl ketones, and alcohols which are oxidized to methyl ketones, will give a positive iodoform test. All of the compounds in this problem except pentan-3-one (part (d)) will give a positive iodoform test.

22-10



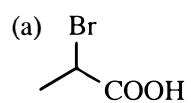
22-11



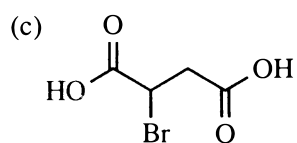
from Solved Problem 22-2

E2 elimination

22-12

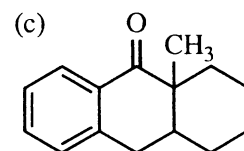
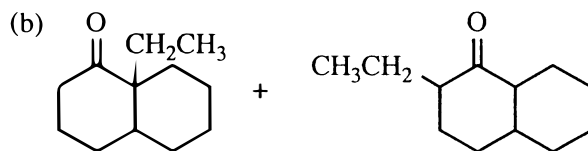
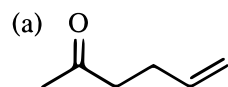


(b) no reaction:
no α -hydrogen

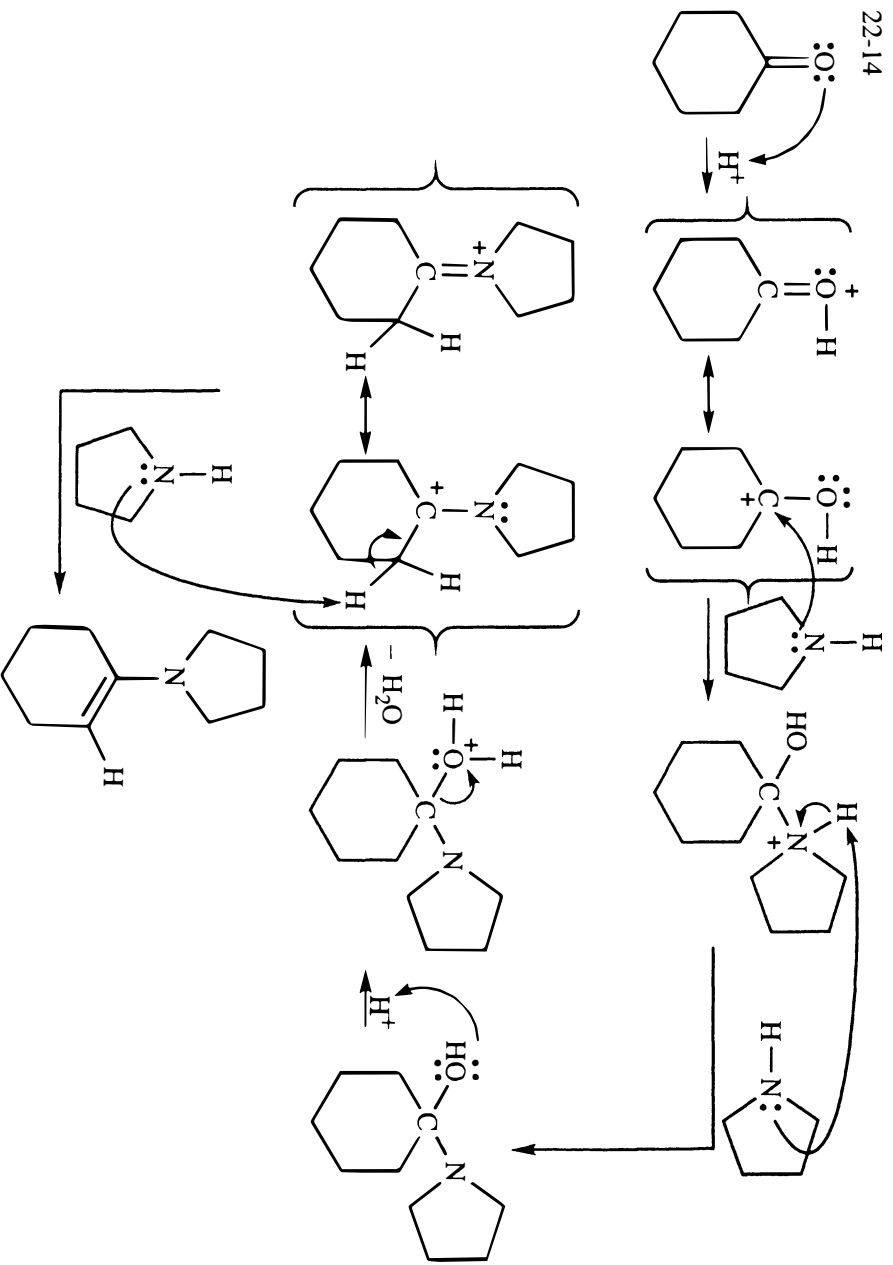


(d) no reaction:
no α -hydrogen

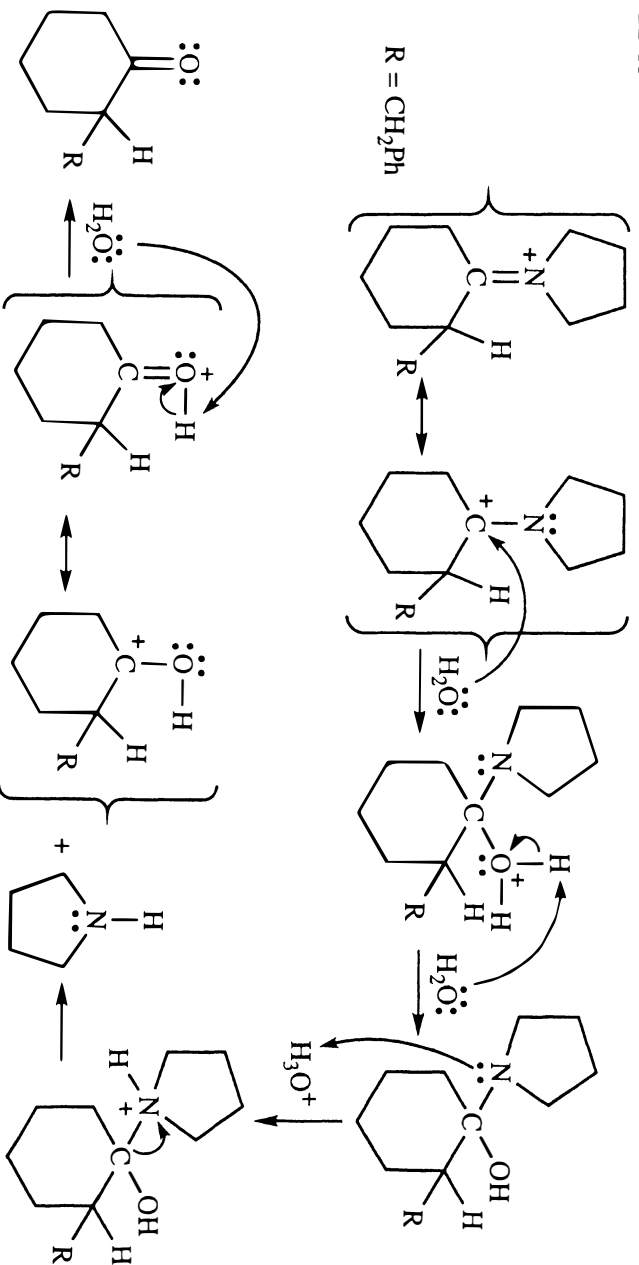
22-13



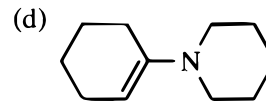
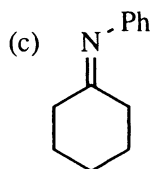
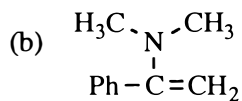
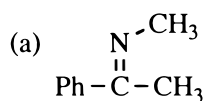
22-14



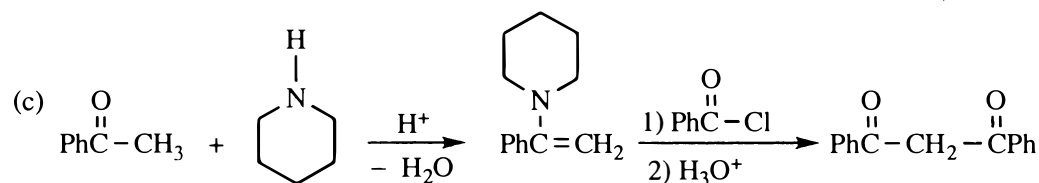
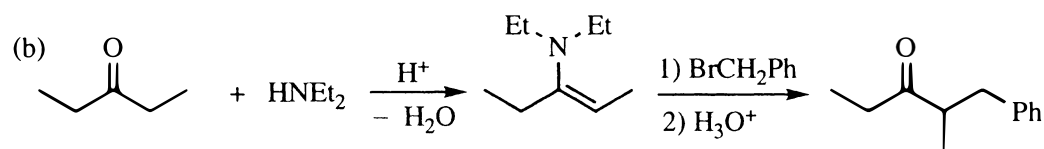
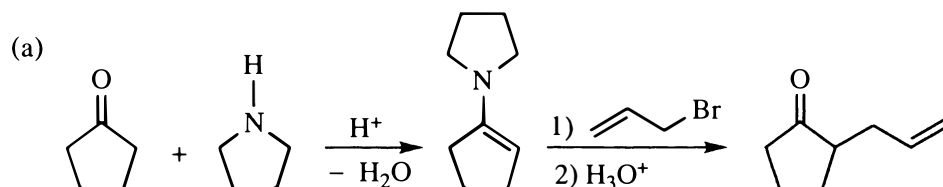
22-15



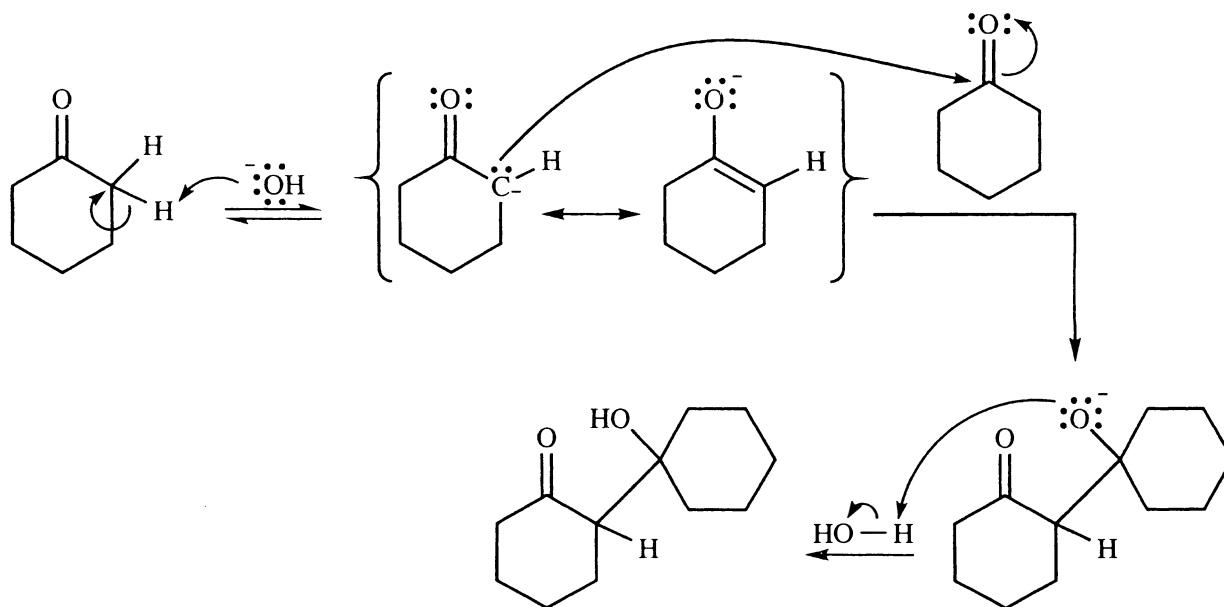
22-16



22-17 Any 2° aliphatic amines can be used for this problem.



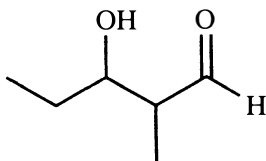
22-18



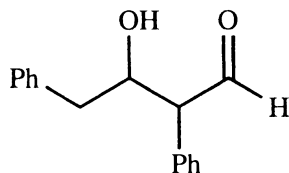
In general, the equilibrium in aldol condensations of ketones favors reactants rather than products. There is significant steric hindrance at both carbons with new bonds, so it is reasonable to conclude that this reaction of cyclohexanone would also favor reactants at equilibrium.

22-19

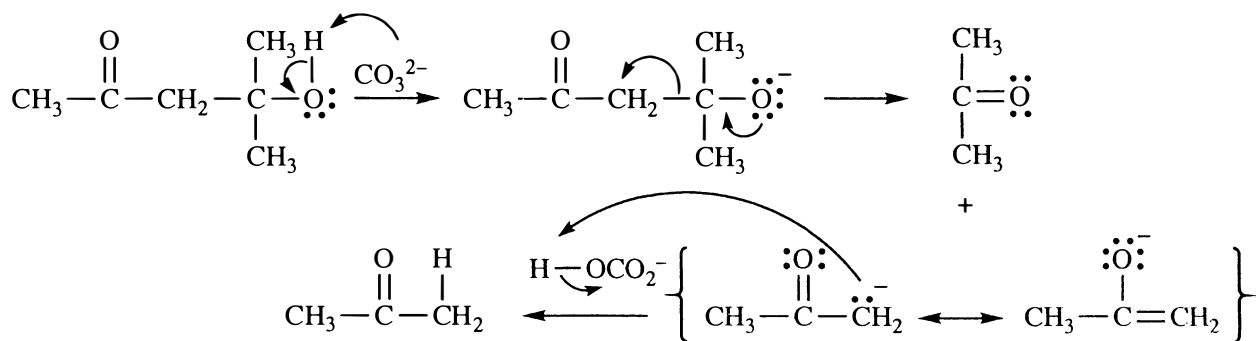
(a)



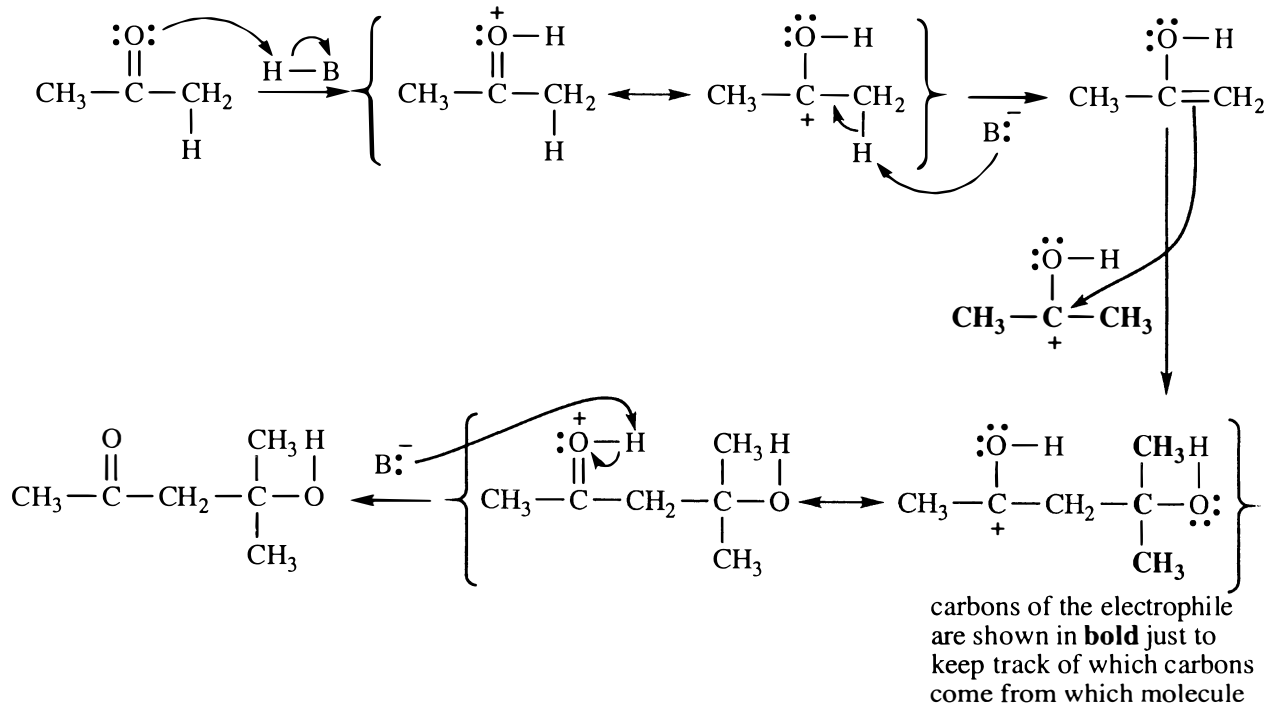
(b)



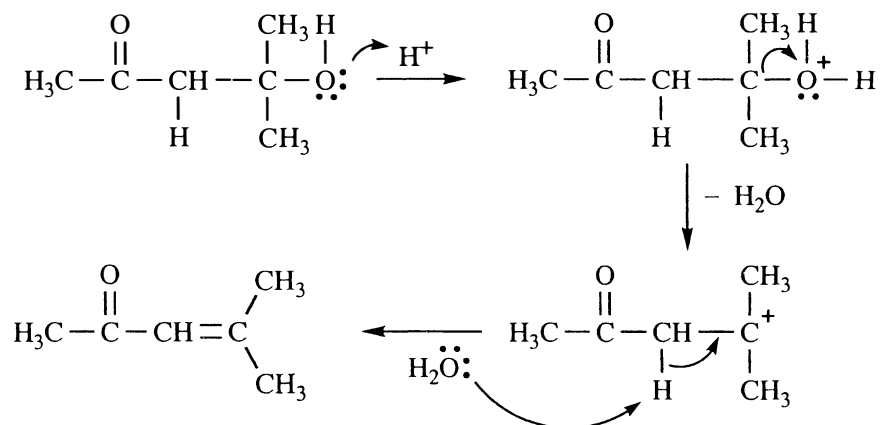
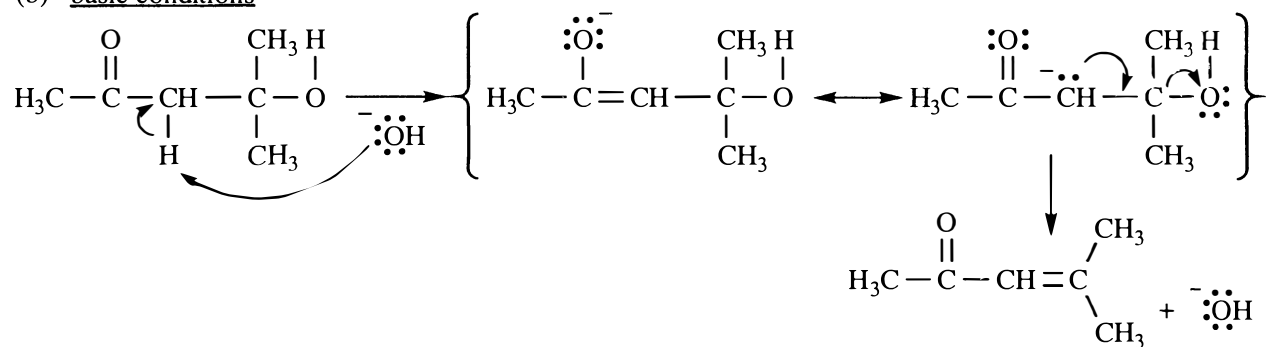
22-20 All the steps in the aldol condensation are reversible. Adding base to diacetone alcohol promoted the reverse aldol reaction. The equilibrium greatly favors acetone.



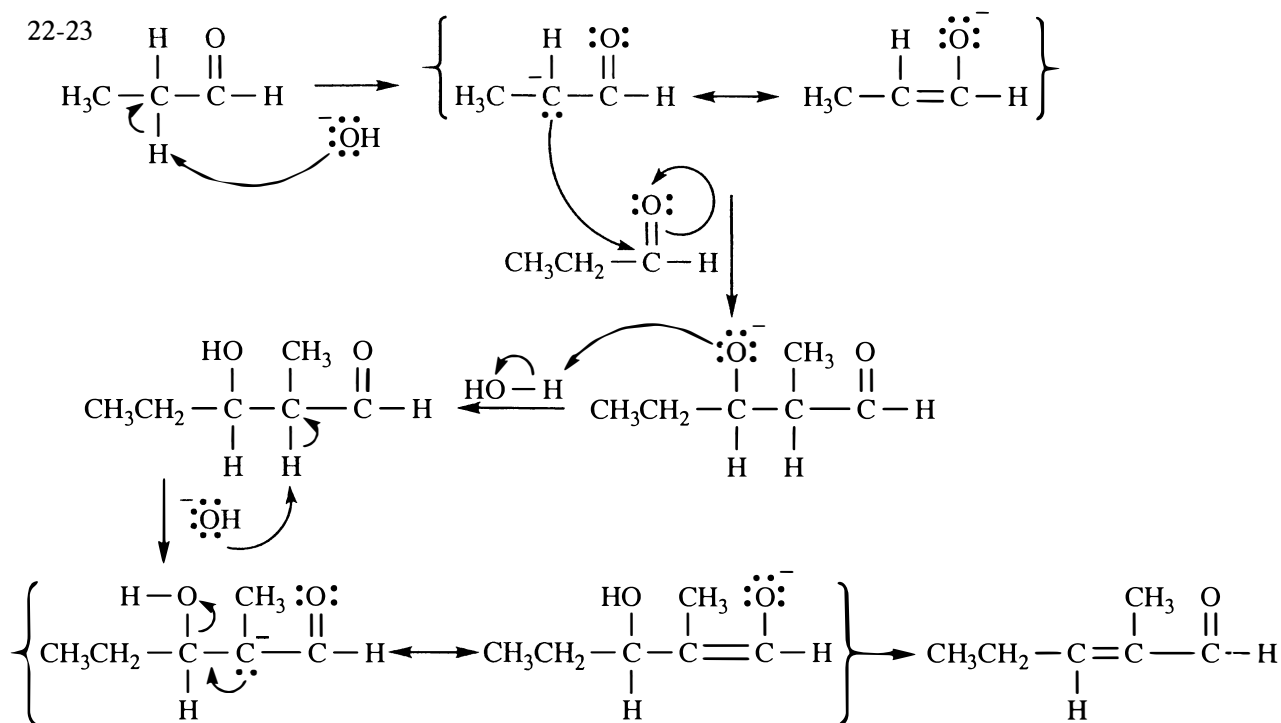
22-21



22-22

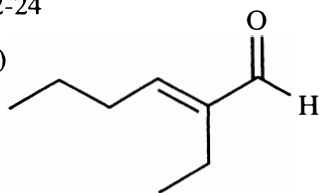
(a) acidic conditions(b) basic conditions

22-23

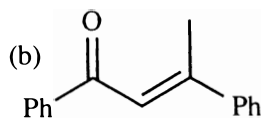


22-24

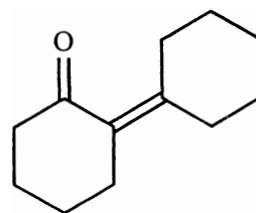
(a)



(b)



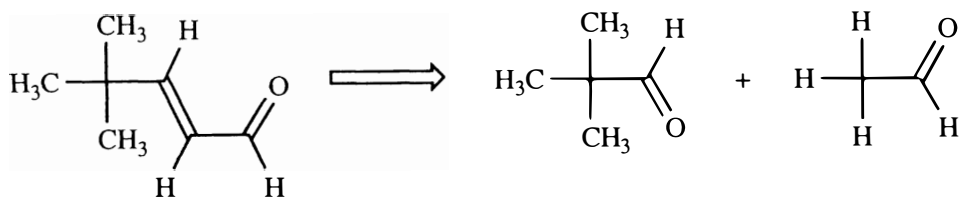
(c)



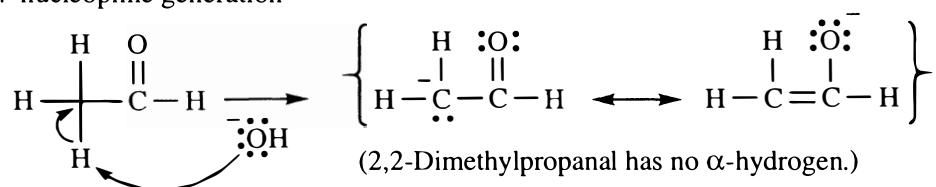
22-25

(a)

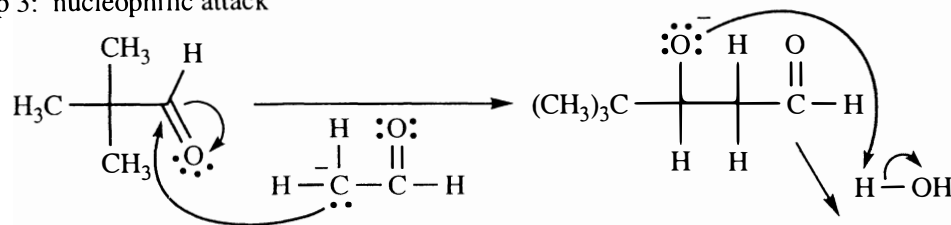
Step 1: carbon skeletons



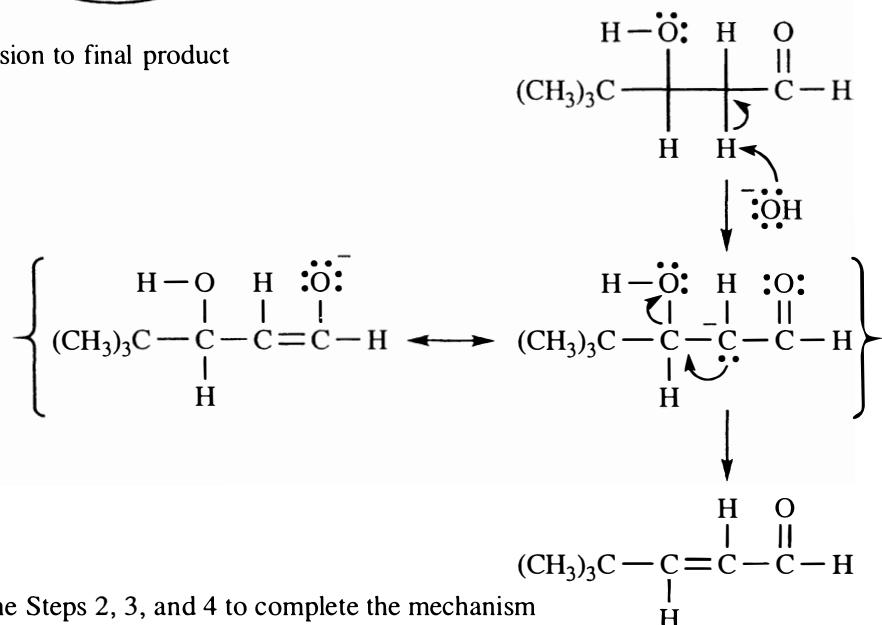
Step 2: nucleophile generation



Step 3: nucleophilic attack



Step 4: conversion to final product

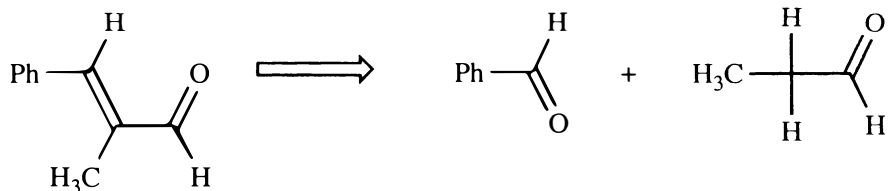


Step 5: combine Steps 2, 3, and 4 to complete the mechanism

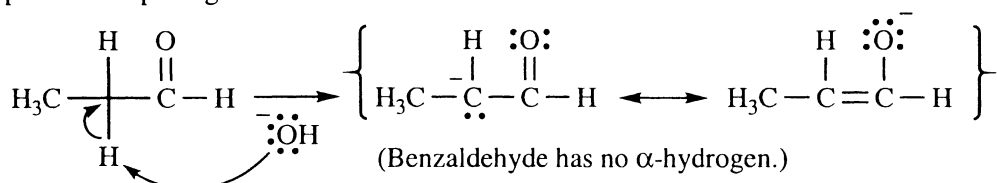
22-25 continued

(b)

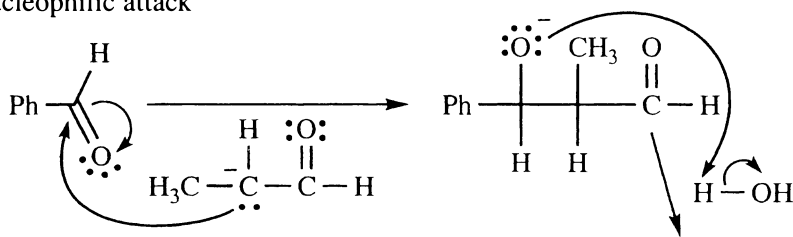
Step 1: carbon skeletons



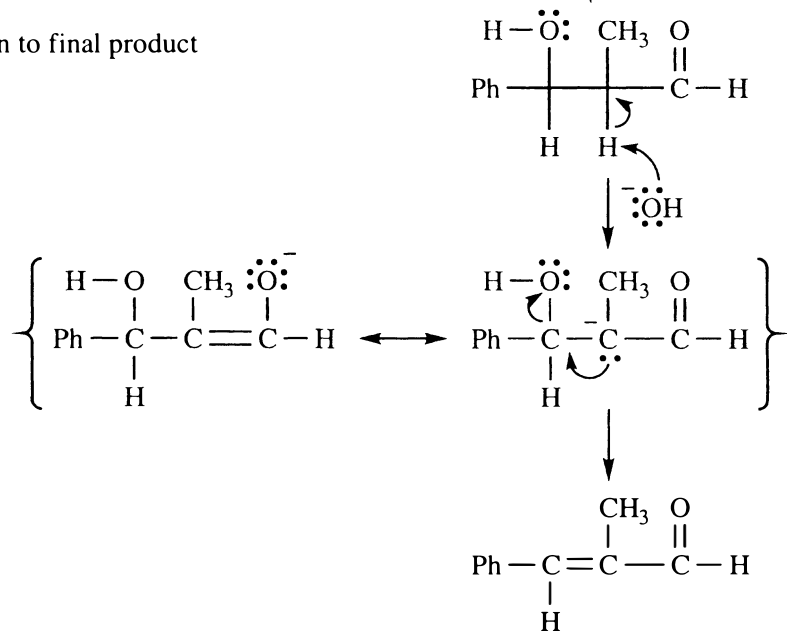
Step 2: nucleophile generation



Step 3: nucleophilic attack



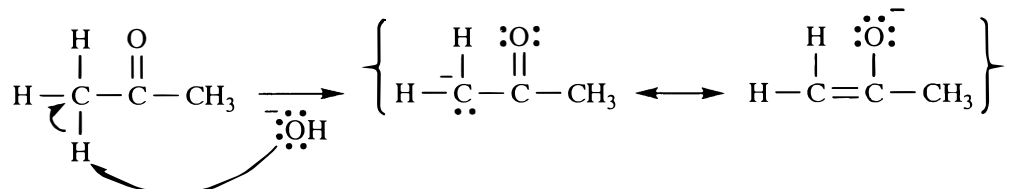
Step 4: conversion to final product



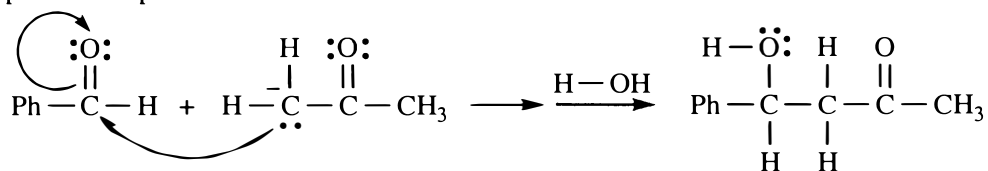
Step 5: combine Steps 2, 3, and 4 to complete the mechanism

22-26 This solution presents the sequence of reactions leading to the product, following the format of the Problem-Solving feature. This is not a complete mechanism.

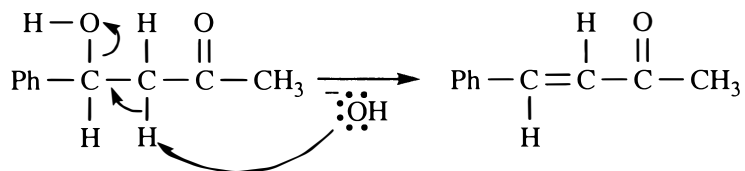
Step 2: generation of the nucleophile



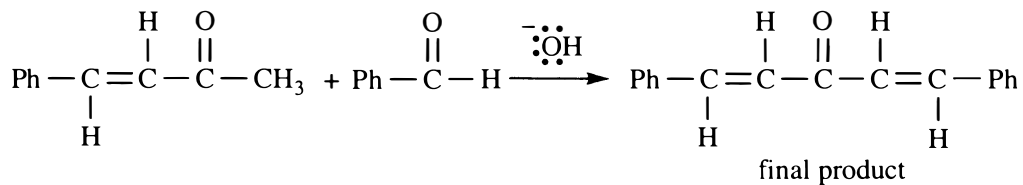
Step 3: nucleophilic attack



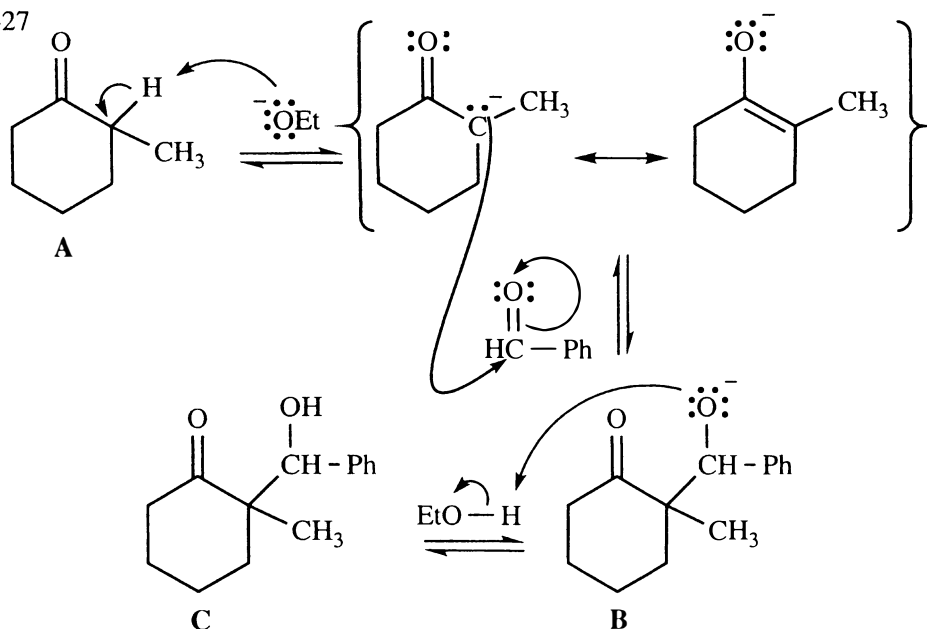
Step 4: dehydration



The same sequence of steps occurs on the other side.



22-27

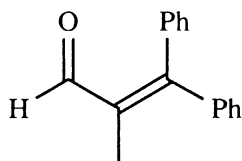


There are three problems with the reaction as shown:

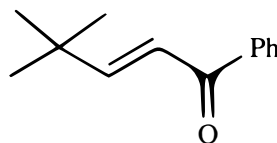
1. Hydrogen on a 3° carbon (structure A) is less acidic than hydrogen on a 2° carbon. The 3° hydrogen will be removed at a slower rate than the 2° hydrogen.
2. Nucleophilic attack by the 3° carbon will be more hindered, and therefore slower, than attack by the 2° carbon. Structure B is quite hindered.
3. Once a normal aldol product is formed, dehydration gives a conjugated system which has great stability. The aldol product C cannot dehydrate because no α -hydrogen remains. Some C will form, but eventually the reverse-aldol process will return C to starting materials which, in turn, will react at the other α -carbon to produce the conjugated system. (This reason is the Kiss of Death for C.)

22-28

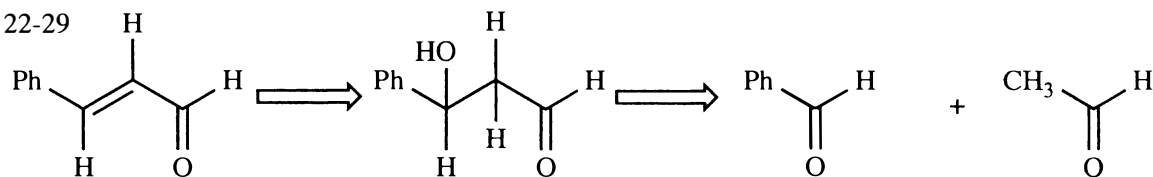
(a)



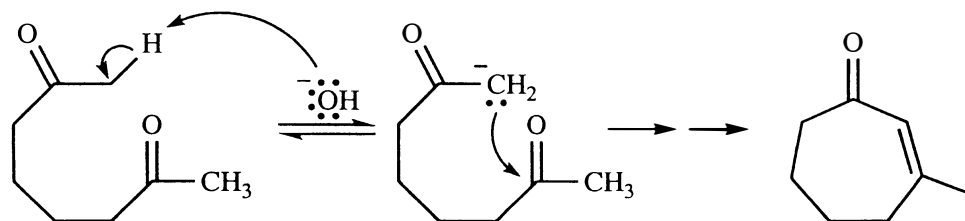
(b)



22-29

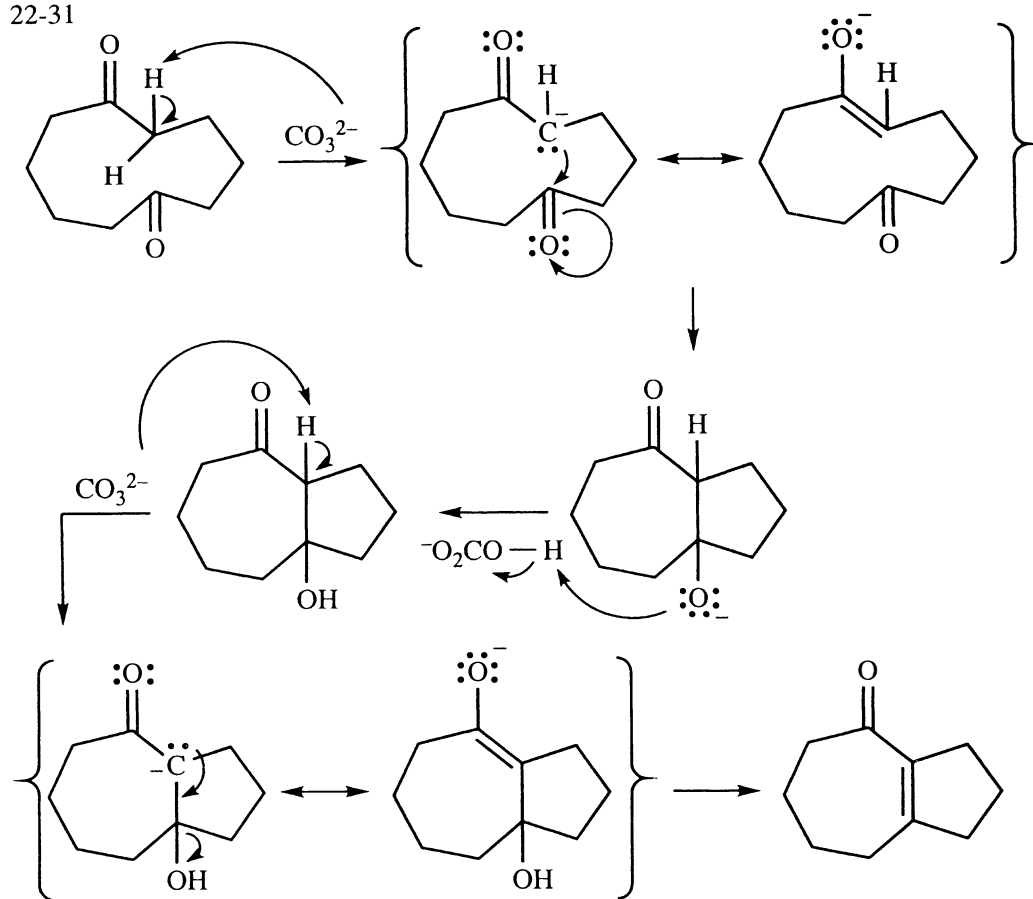


22-30

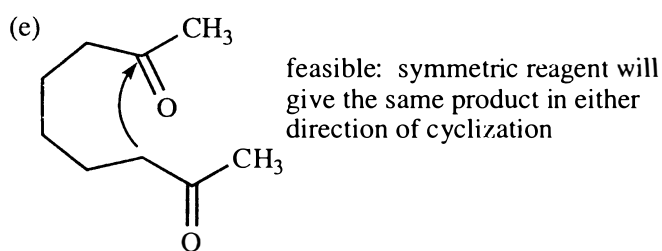
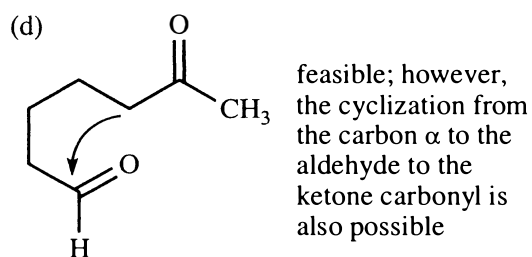
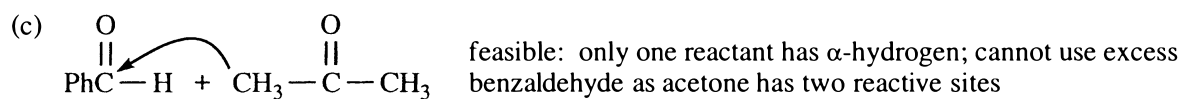
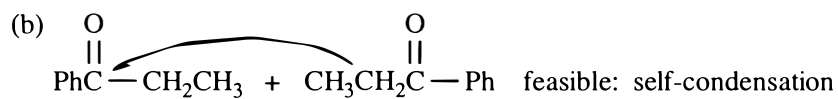
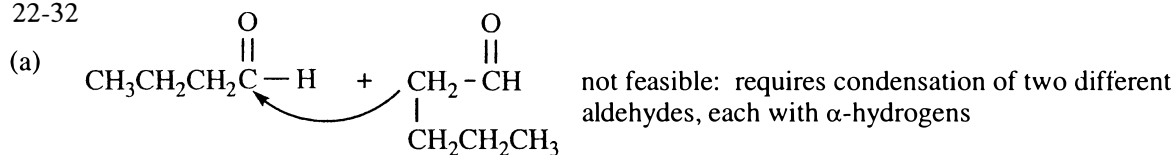


The formation of a seven-membered ring is unfavorable for entropy reasons: the farther apart the nucleophile and the electrophile, the harder time they will have finding each other. If the molecule has a possibility of forming a 5- or a 7-membered ring, it will almost always prefer to form the 5-membered ring.

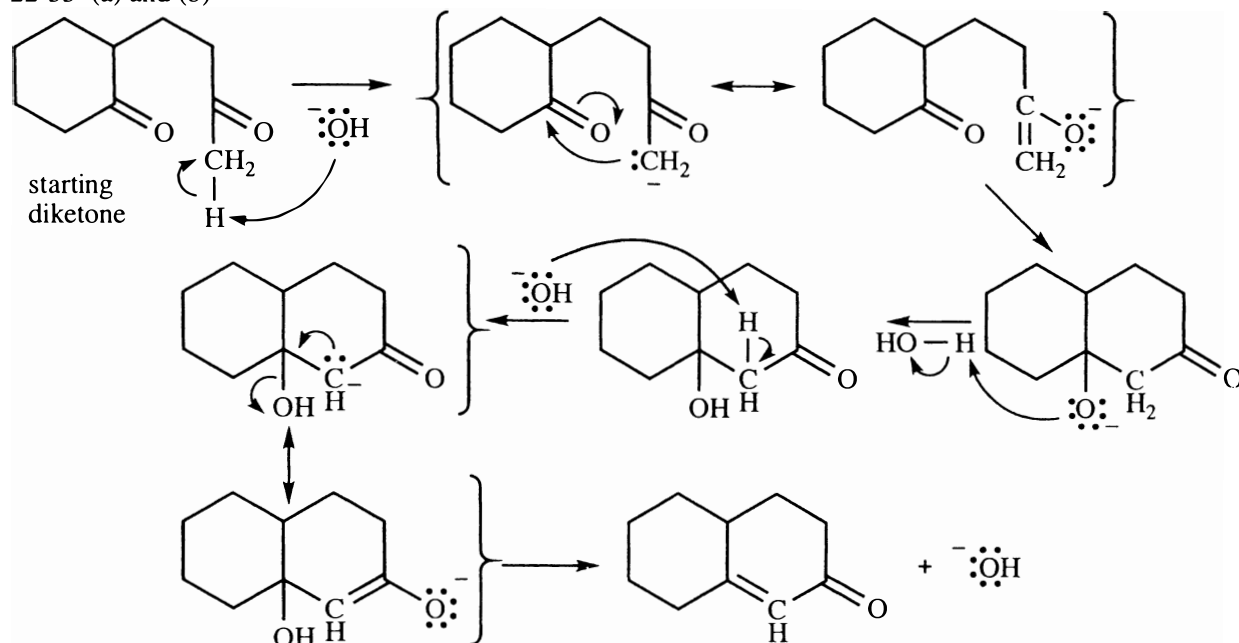
22-31



22-32

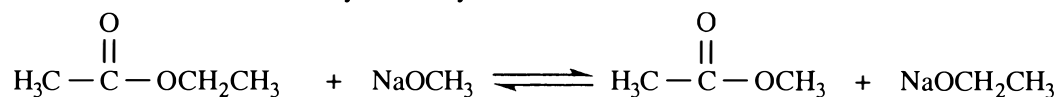


22-33 (a) and (b)



22-34

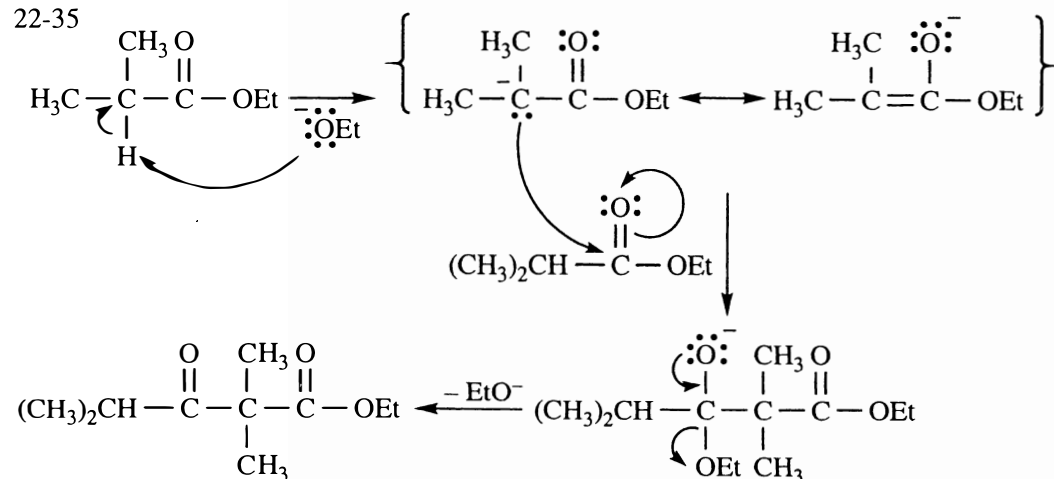
(a) The side reaction with sodium methoxide is transesterification. The starting material, and therefore the product, would be a mixture of methyl and ethyl esters.



(b) Sodium hydroxide would irreversibly saponify the ester, completely stopping the Claisen condensation as the carbonyl no longer has a leaving group attached to it.



22-35

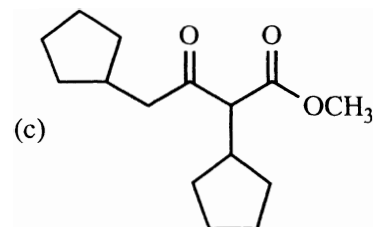
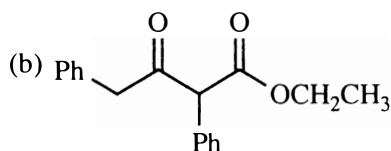
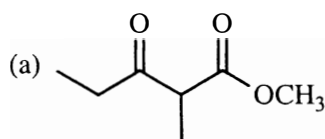


explanation on next page

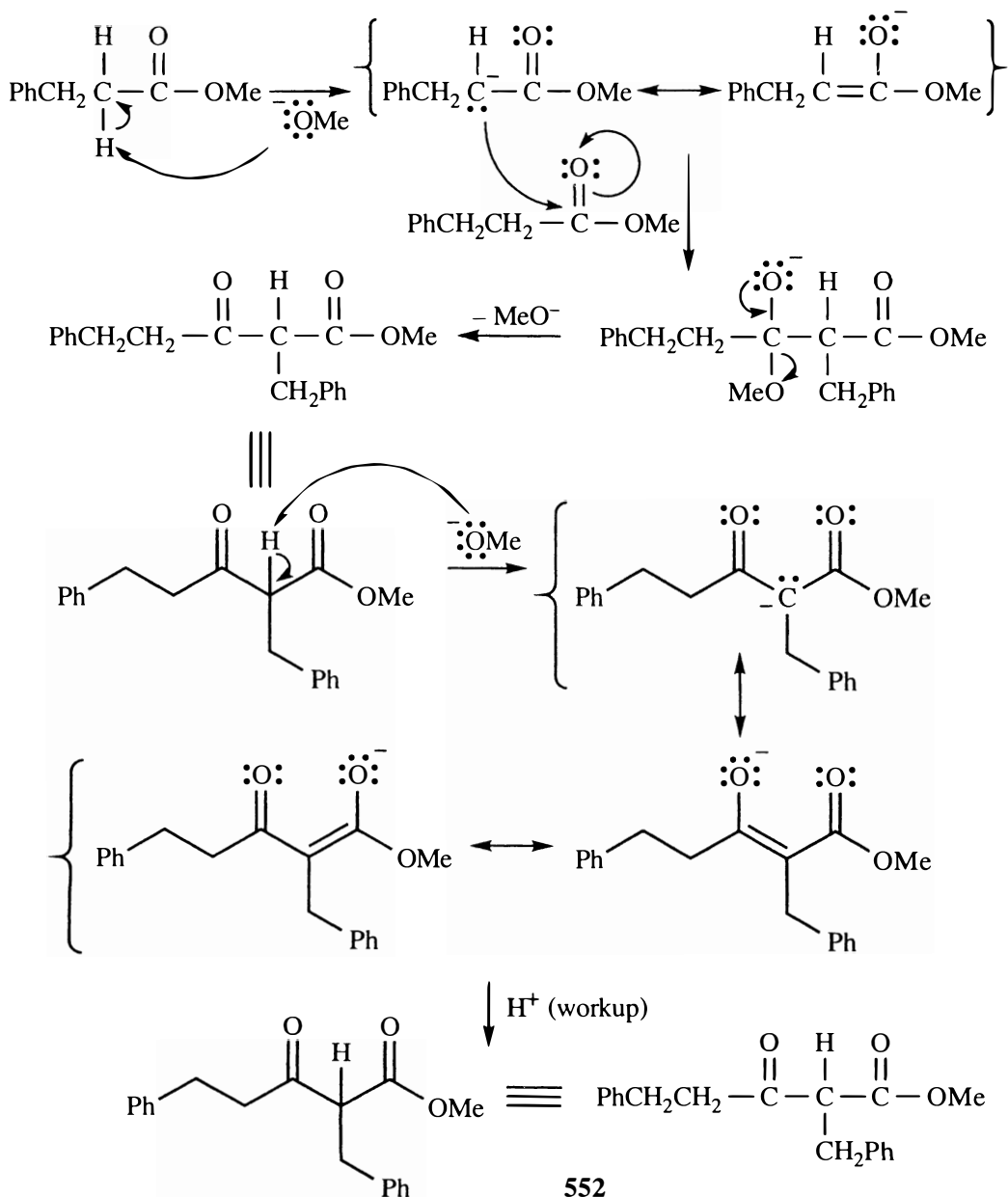
22-35 continued

There are two reasons why this reaction gives a poor yield. The nucleophilic carbon in the enolate is 3° and attack is hindered. More important, the final product has no hydrogen on the α-carbon, so the deprotonation by base which is the driving force in other Claisen condensations cannot occur here. What is produced is an *equilibrium mixture* of product and starting materials; the conversion to product is low.

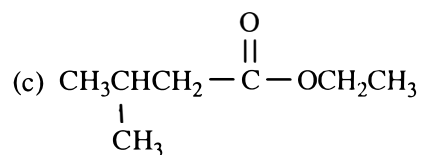
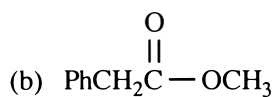
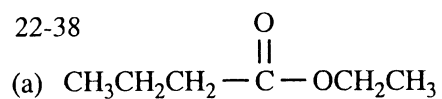
22-36



22-37

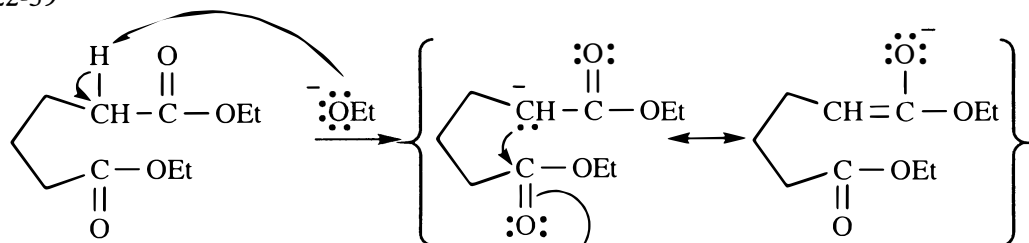


22-38

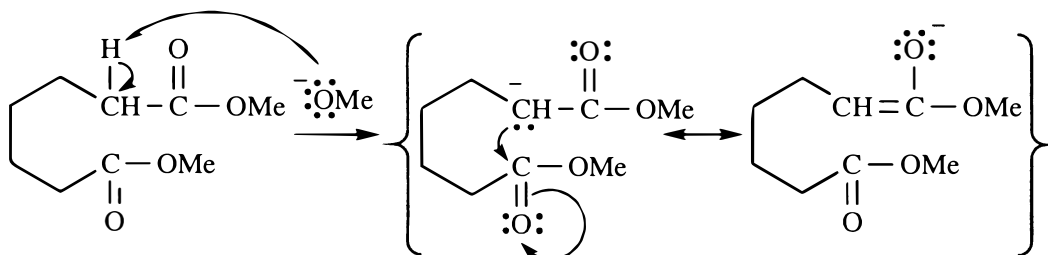
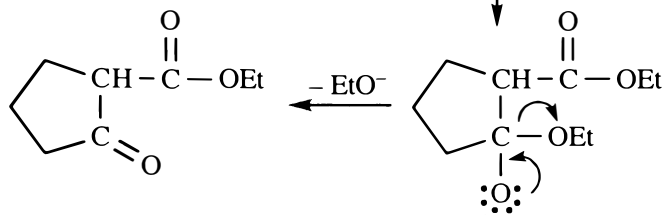


This one would be difficult because the alpha-carbon is hindered.

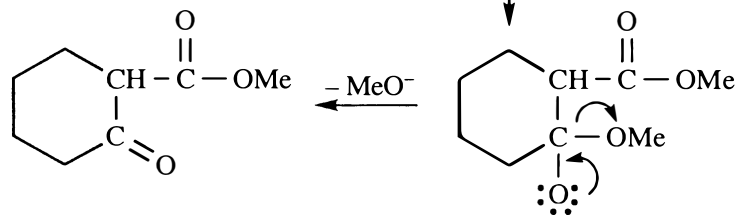
22-39



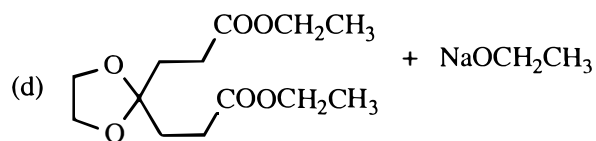
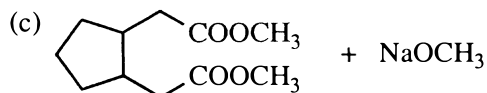
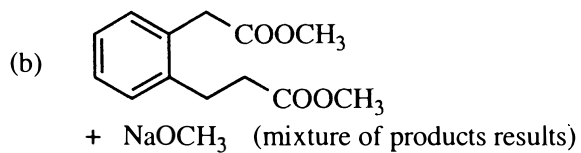
This is the final product, after removal of the α -hydrogen by ethoxide, followed by reprotonation during the workup.



This is the final product, after removal of the α -hydrogen by ethoxide, followed by reprotonation during the workup.

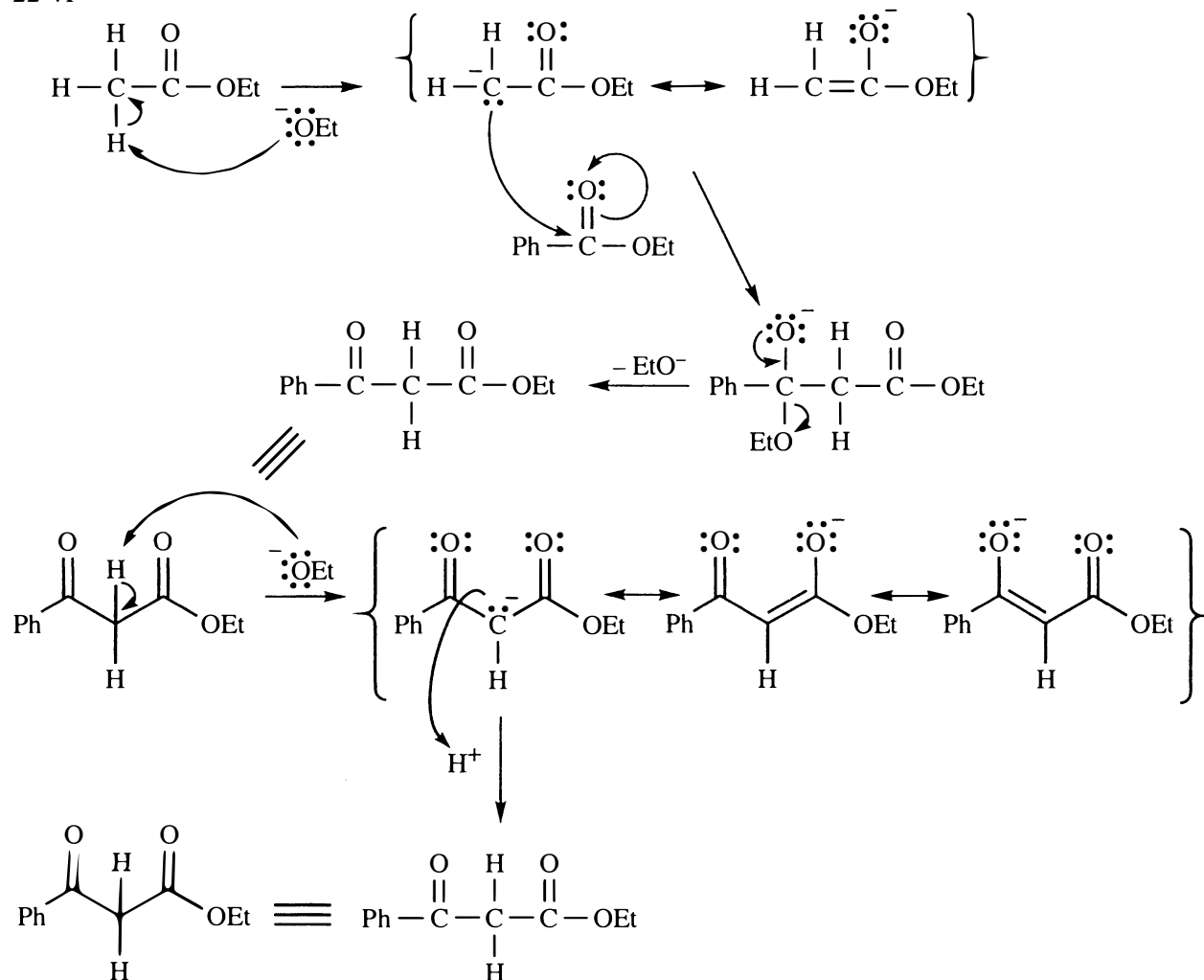


22-40

(a) not possible by Dieckmann—not a β -keto ester

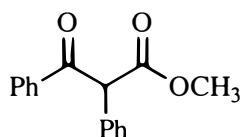
The protecting group is necessary to prevent aldol condensation. Aqueous acid workup removes the protecting group.

22-41

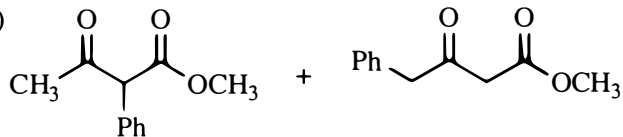


22-42

(a)

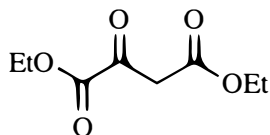


(b)

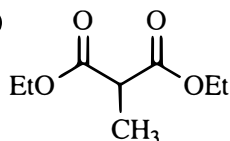


plus 2 self-condensation products—a poor choice
because both esters have α -hydrogens

(c)

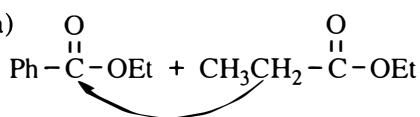


(d)

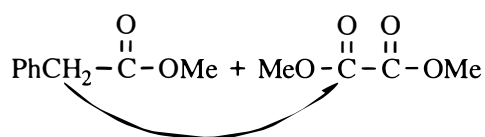


22-43

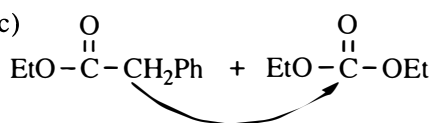
(a)



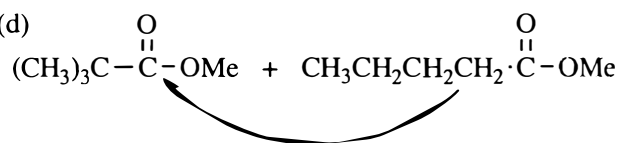
(b)



(c)

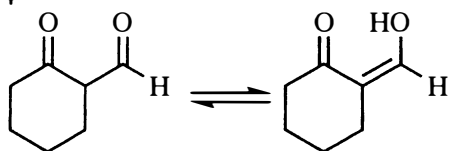


(d)

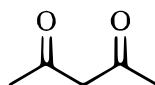


22-44

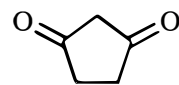
(a)



(b)



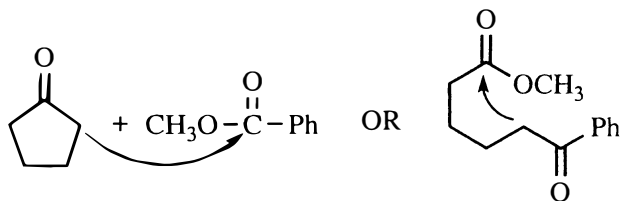
(c)



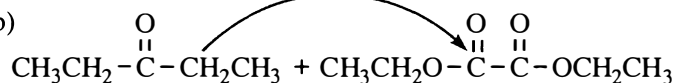
actually present in the enol form:

22-45

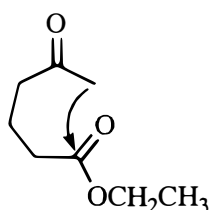
(a) two ways:



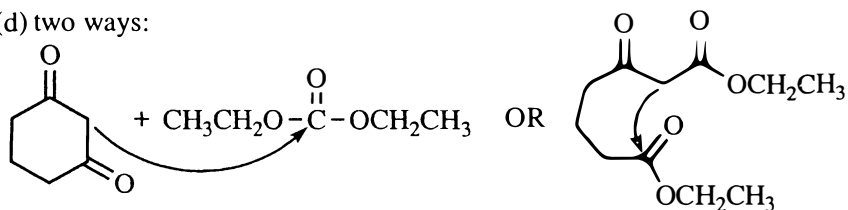
(b)



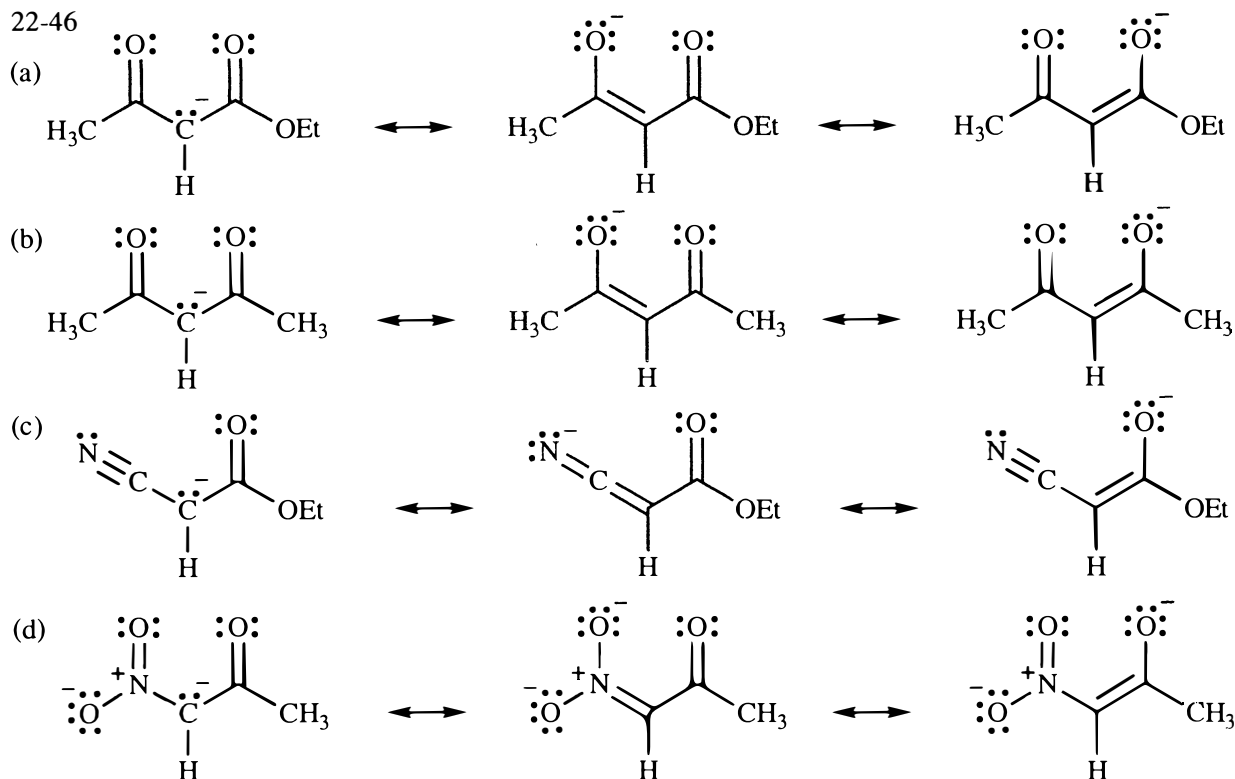
(c)



(d) two ways:

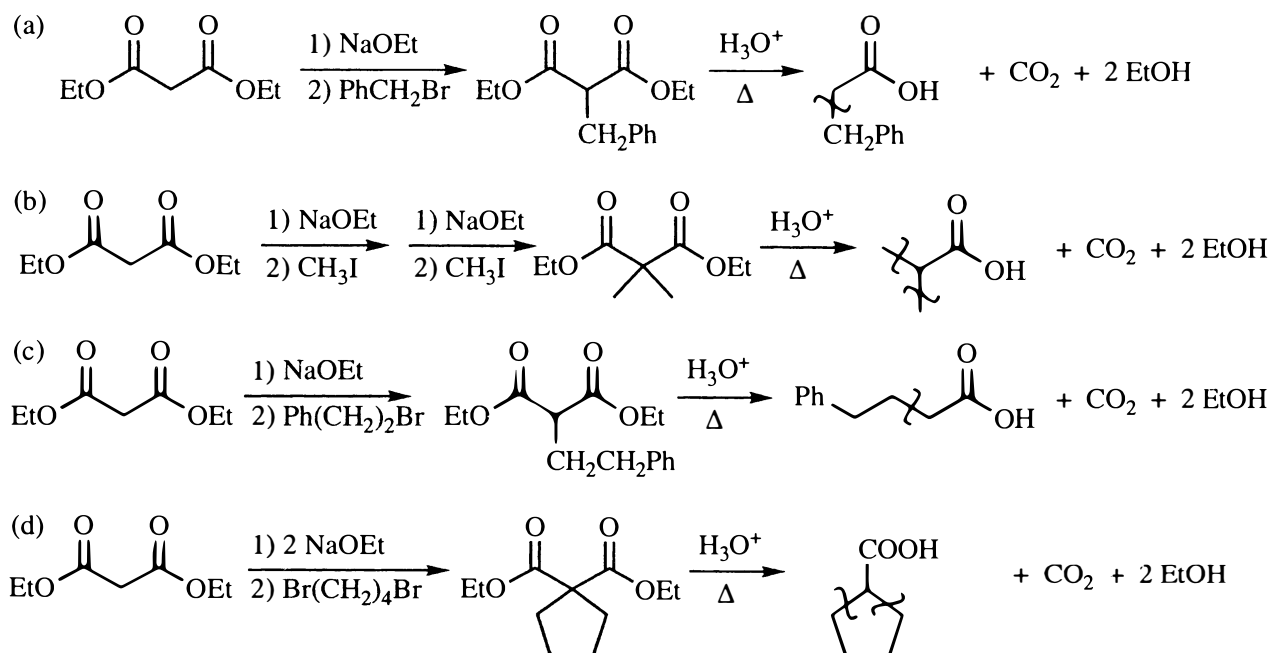


22-46



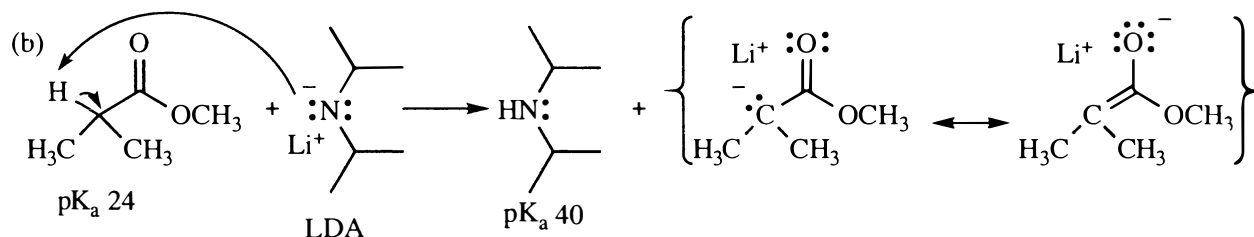
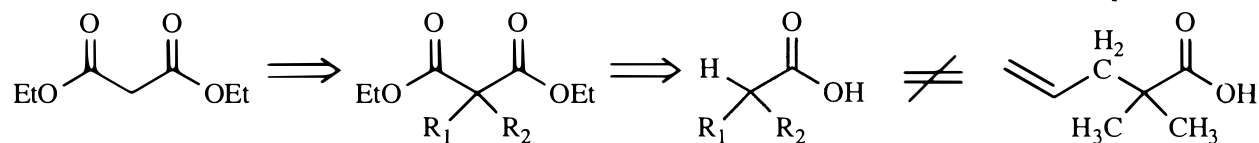
(other resonance forms of the nitro group are not shown)

22-47 In the products, the wavy lines cross the bonds that must be made by alkylation, before hydrolysis and decarboxylation produce the substituted acetic acid.

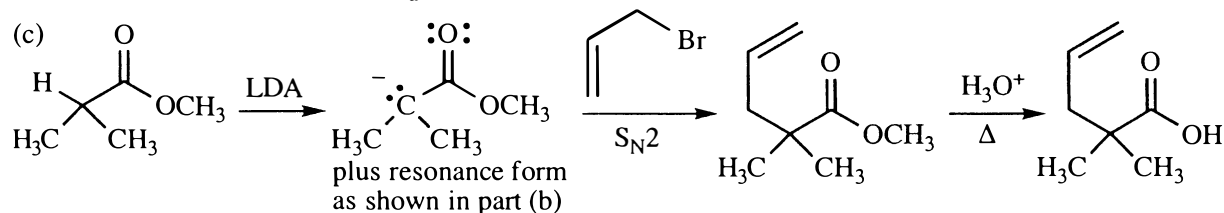


22-48

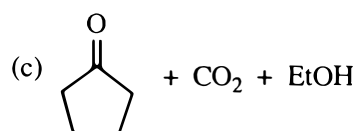
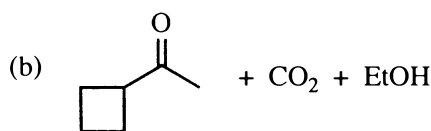
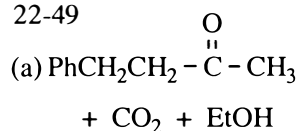
(a) Only two substituent groups plus a hydrogen atom can appear on the alpha carbon after decarboxylation at the end of the malonic ester synthesis. The product shown has three alkyl groups, so it cannot be made by malonic ester synthesis.



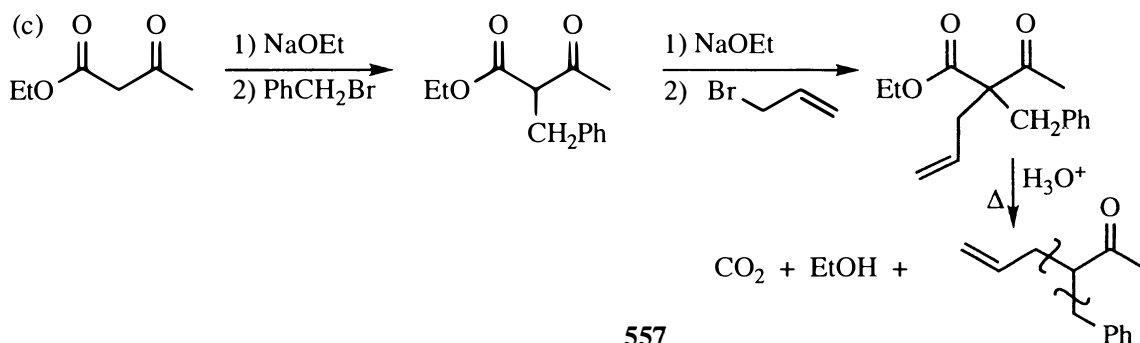
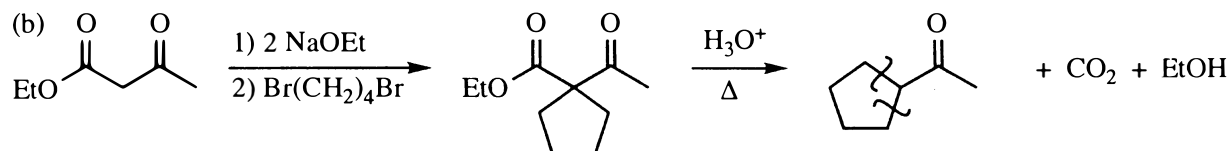
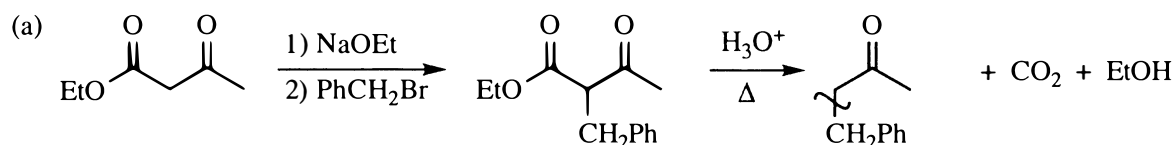
With such a large difference in pK_a values, products are favored $>> 99\%$.



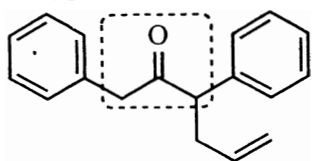
22-49



22-50 In the products, the wavy lines indicate the bonds that must be made by alkylation, before hydrolysis and decarboxylation produce the substituted acetone.

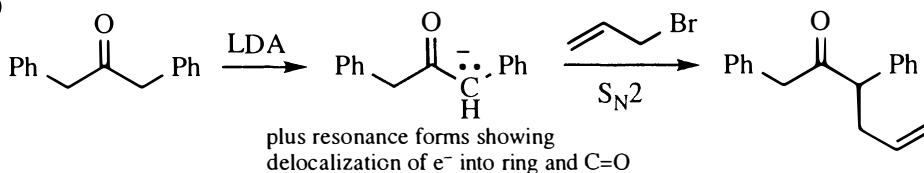


22-51

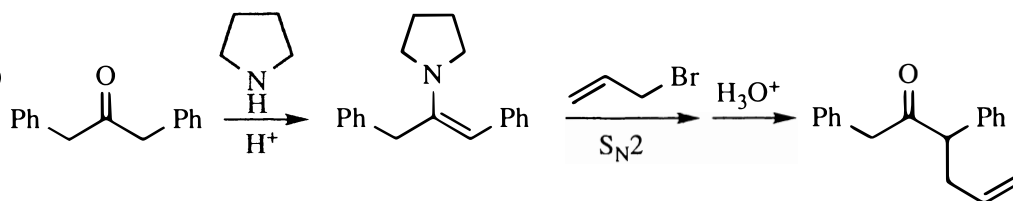


(a) There are two problems with attempting to make this compound by acetoacetic ester synthesis. The acetone "core" of the product is shown in the box. This product would require alkylation at BOTH carbons of the acetone "core" of acetoacetic ester; in reality, only one carbon undergoes alkylation in the acetoacetic ester synthesis. Second, it is not possible to do an S_N2 type reaction on an unsubstituted benzene ring, so neither benzene could be attached by acetoacetic ester synthesis.

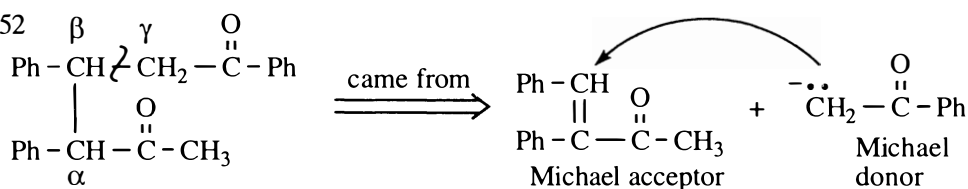
(b)



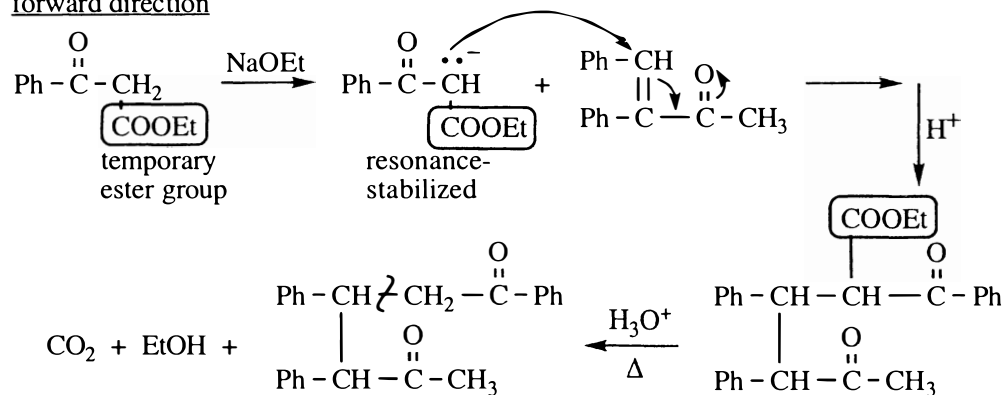
(c)



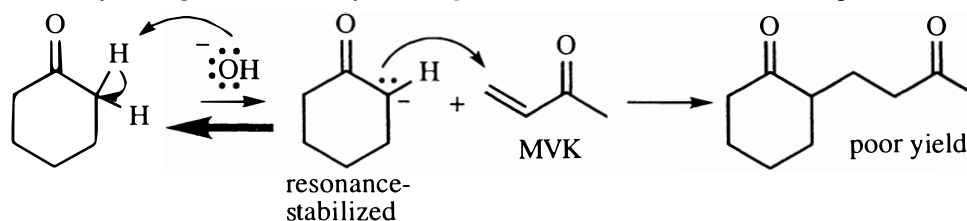
22-52



forward direction



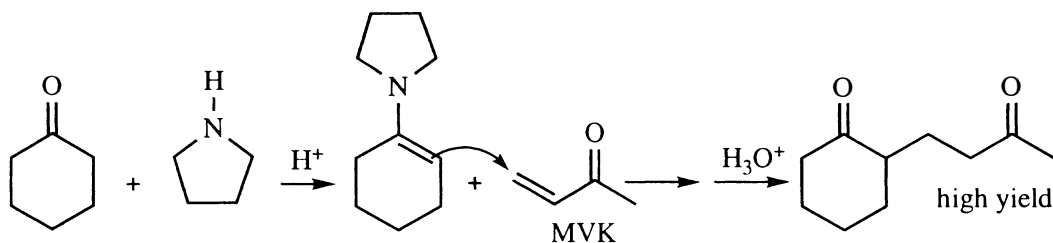
22-53 First, you might wonder why this sequence does not make the desired product:



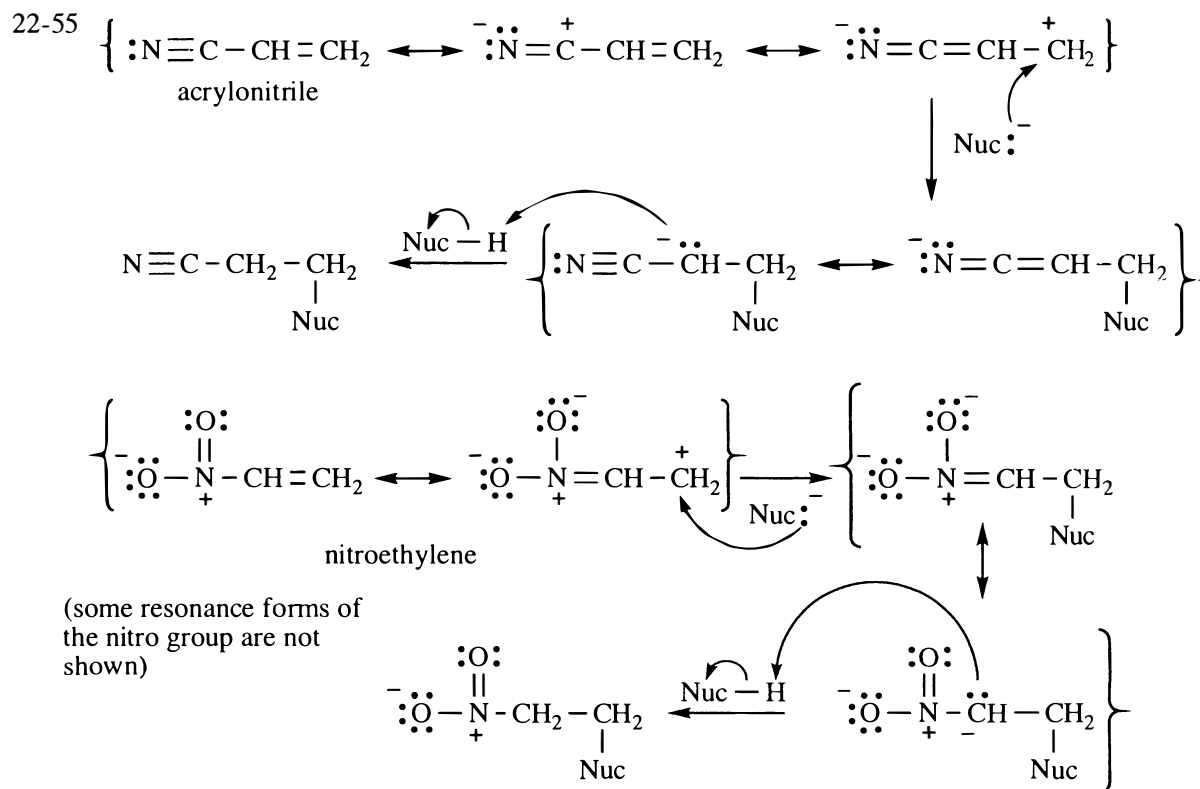
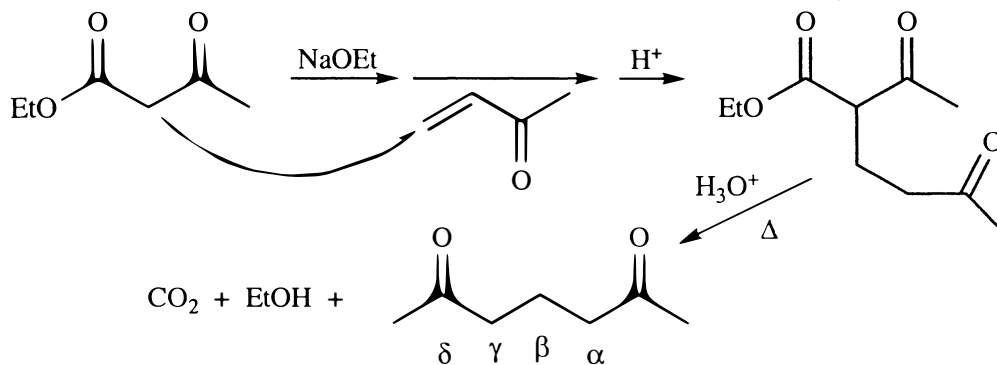
The poor yield in this conjugate addition is due primarily to the numerous competing reactions: the ketone enolate can self-condense (aldol), can condense with the ketone of MVK (aldol), or can deprotonate the methyl of MVK to generate a new nucleophile. The complex mixture of products makes this route practically useless. (continued on next page)

22-53 continued

What permits enamines (or other stabilized enolates) to work are: a) the certainty of which atom is the nucleophile, and b) the lack of self-condensation. Enamines can also do conjugate addition:

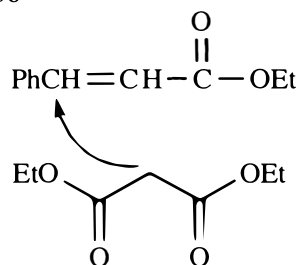


22-54 The enolate of acetoacetic ester can be used in a Michael addition to an α,β -unsaturated ketone like MVK.

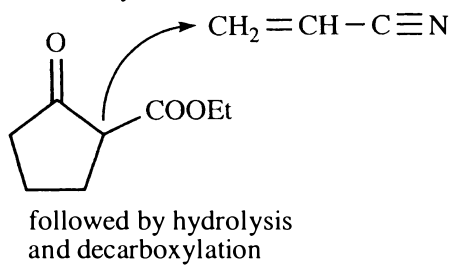


22-56

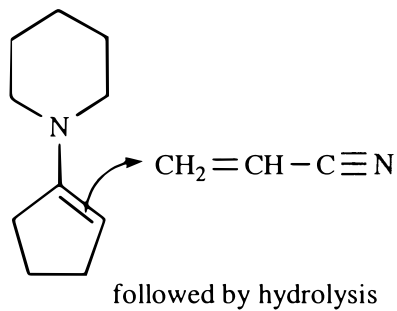
(a)



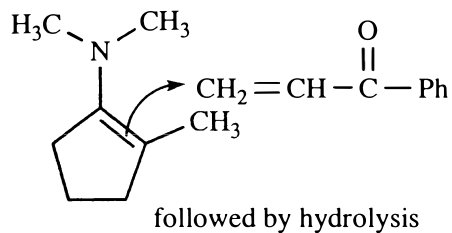
(c) two ways



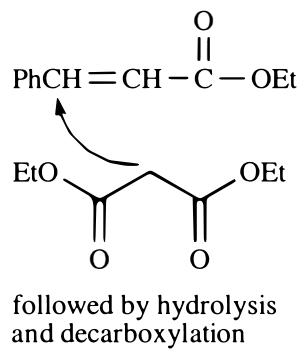
OR



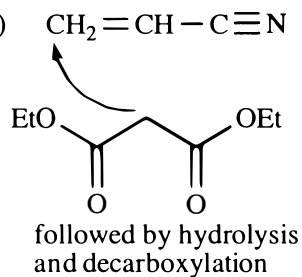
(d)



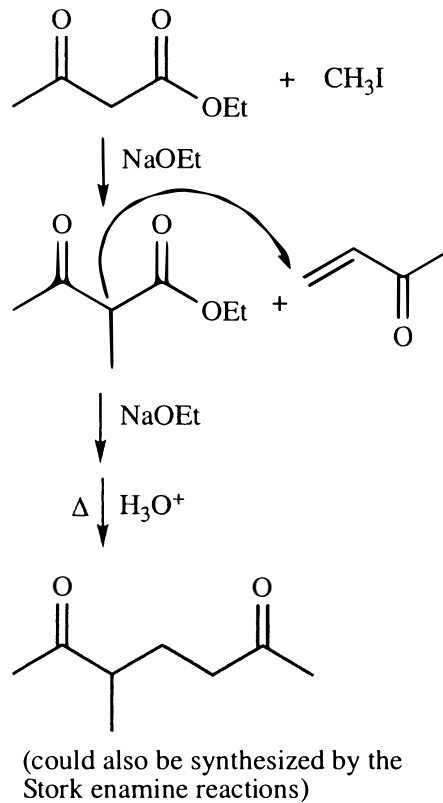
(f)



(b)

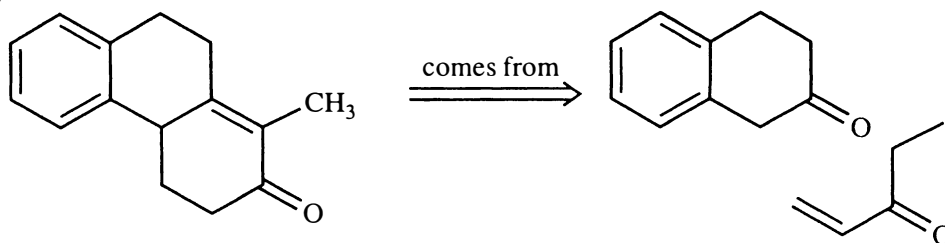


(e)

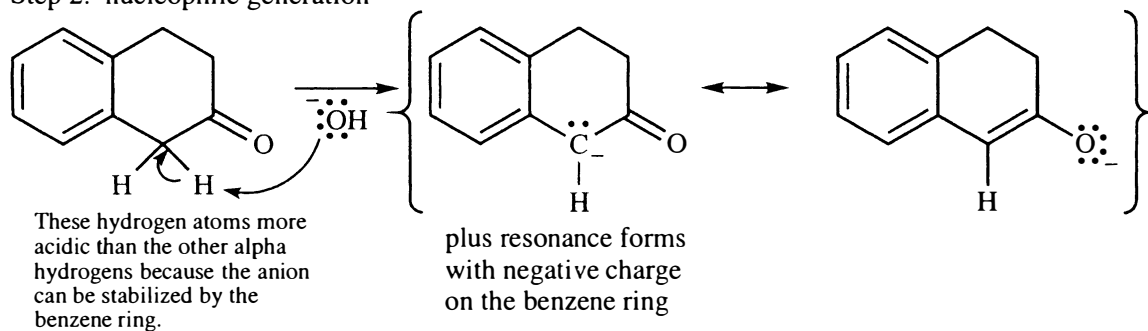


22-57

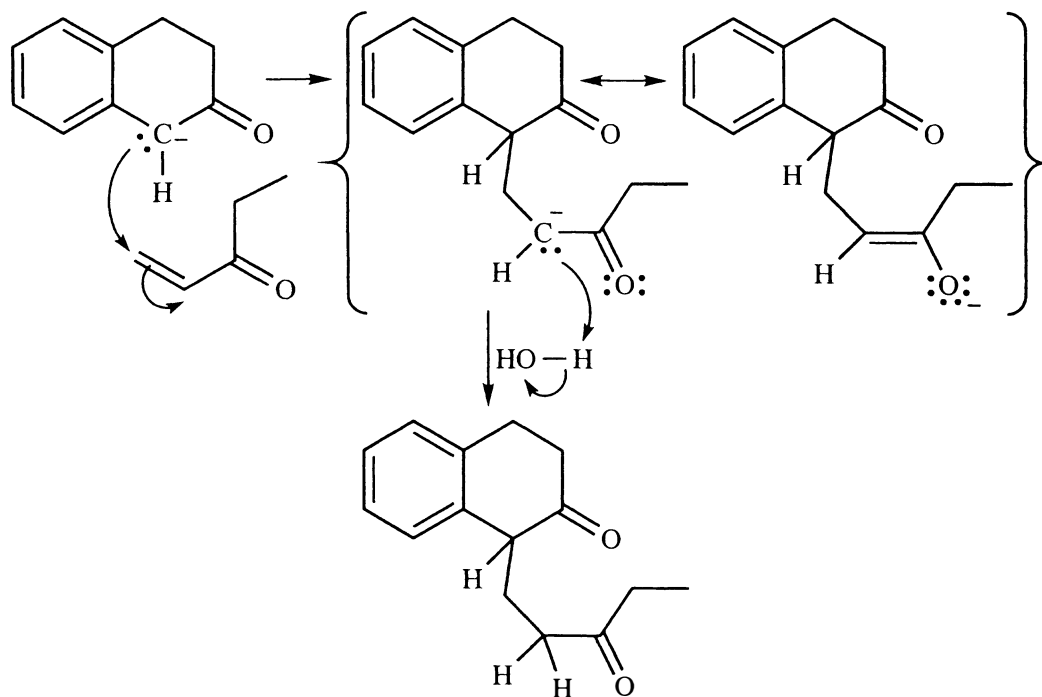
Step 1: carbon skeleton



Step 2: nucleophile generation



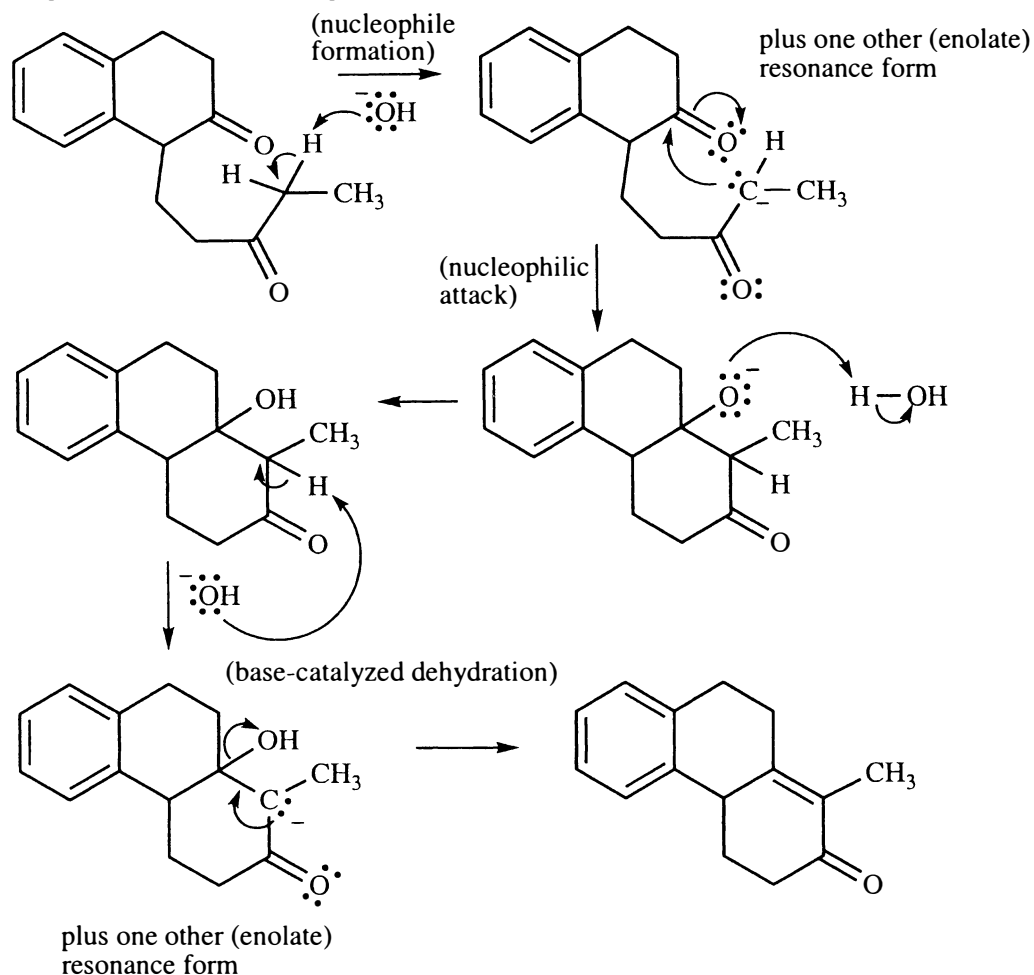
Step 3: nucleophilic attack (Michael addition)



continued on next page

22-57 continued

Step 4: conversion to final product

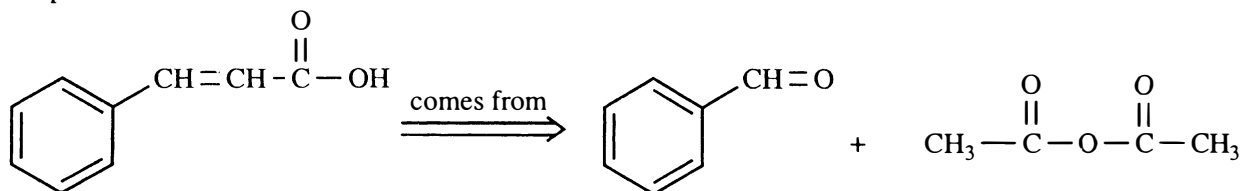


Step 5: The complete mechanism is the combination of Steps 2, 3, and 4. Notice that this mechanism is simply described by:

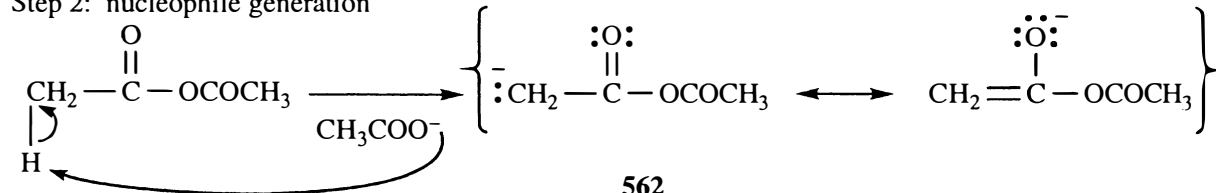
- 1) Enolate formation, followed by Michael addition;
- 2) Aldol condensation, followed by dehydration.

22-58

Step 1: carbon skeleton

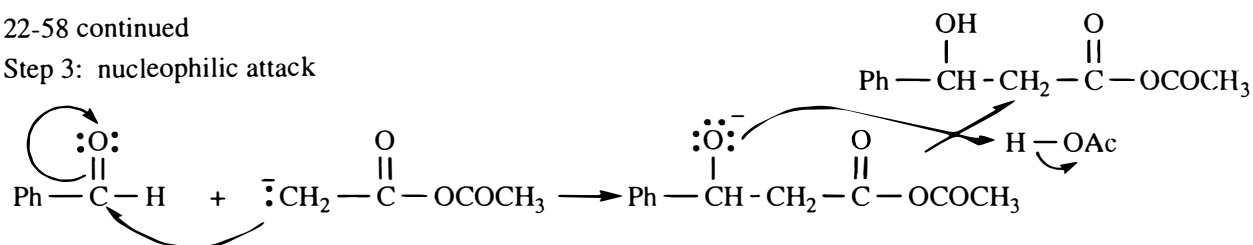


Step 2: nucleophile generation

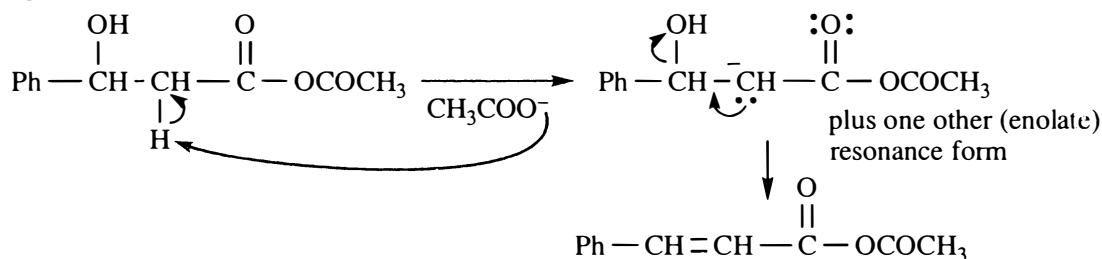


22-58 continued

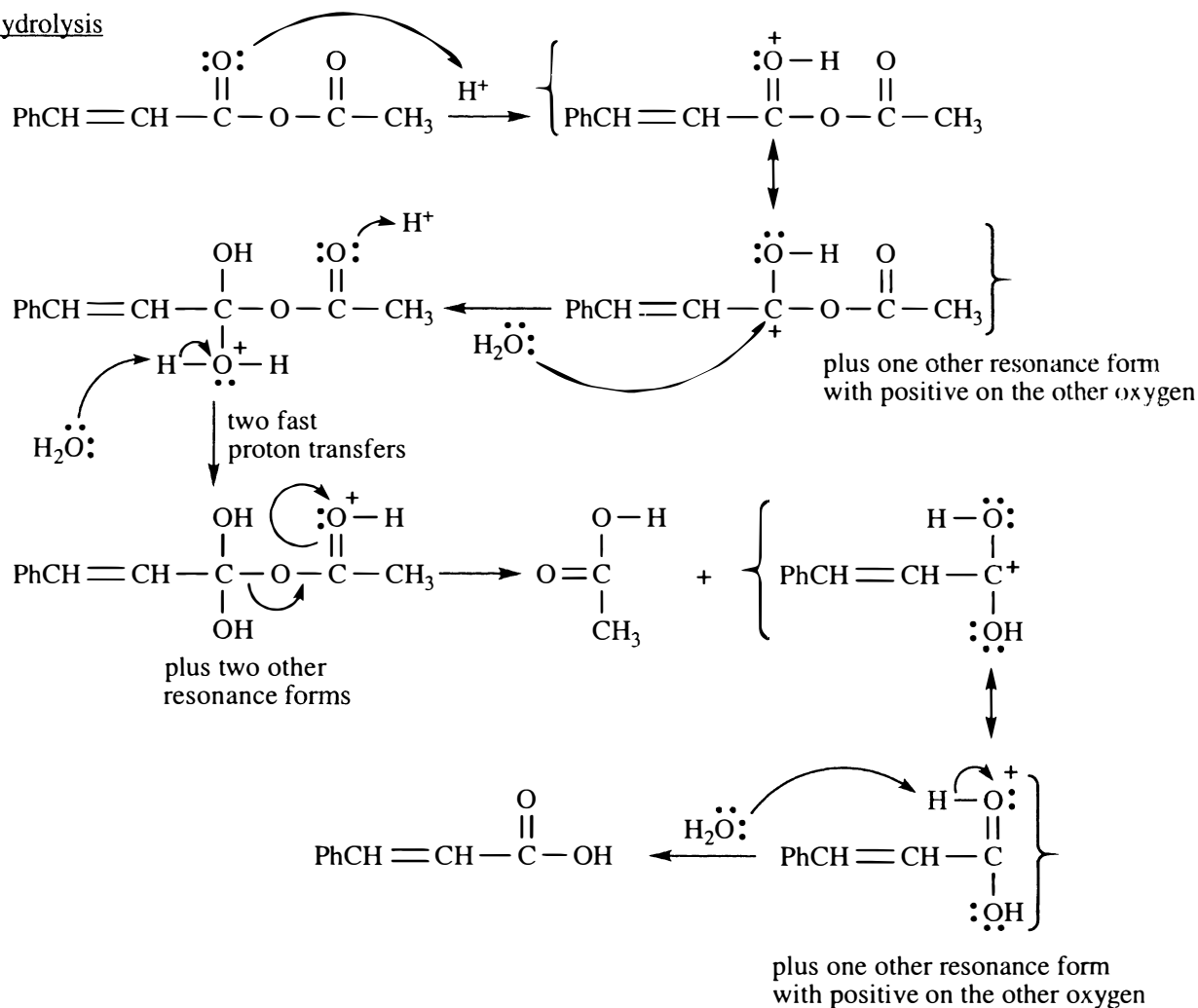
Step 3: nucleophilic attack



Step 4: conversion to final product



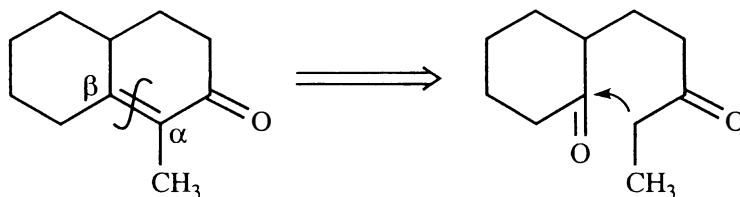
hydrolysis



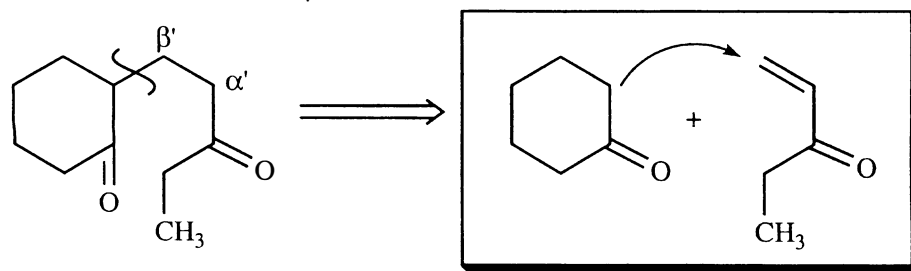
Step 5: The complete mechanism is the combination of Steps 2, 3, and 4.

22-59 The Robinson annulation consists of a Michael addition followed by aldol cyclization with dehydration. In the retrosynthetic direction, disconnect the alkene formed in the aldol/dehydration, then disconnect the Michael addition to discover the reactants.

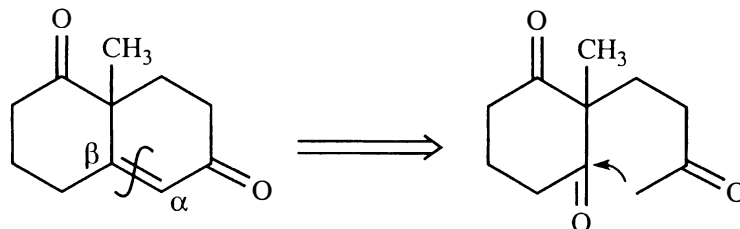
(a) aldol and dehydration forms the α,β double bond:



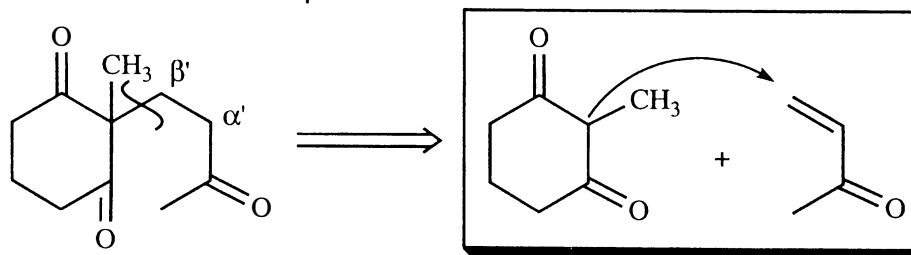
Michael addition forms a bond to the β' carbon:



(b) aldol and dehydration forms the α,β double bond:

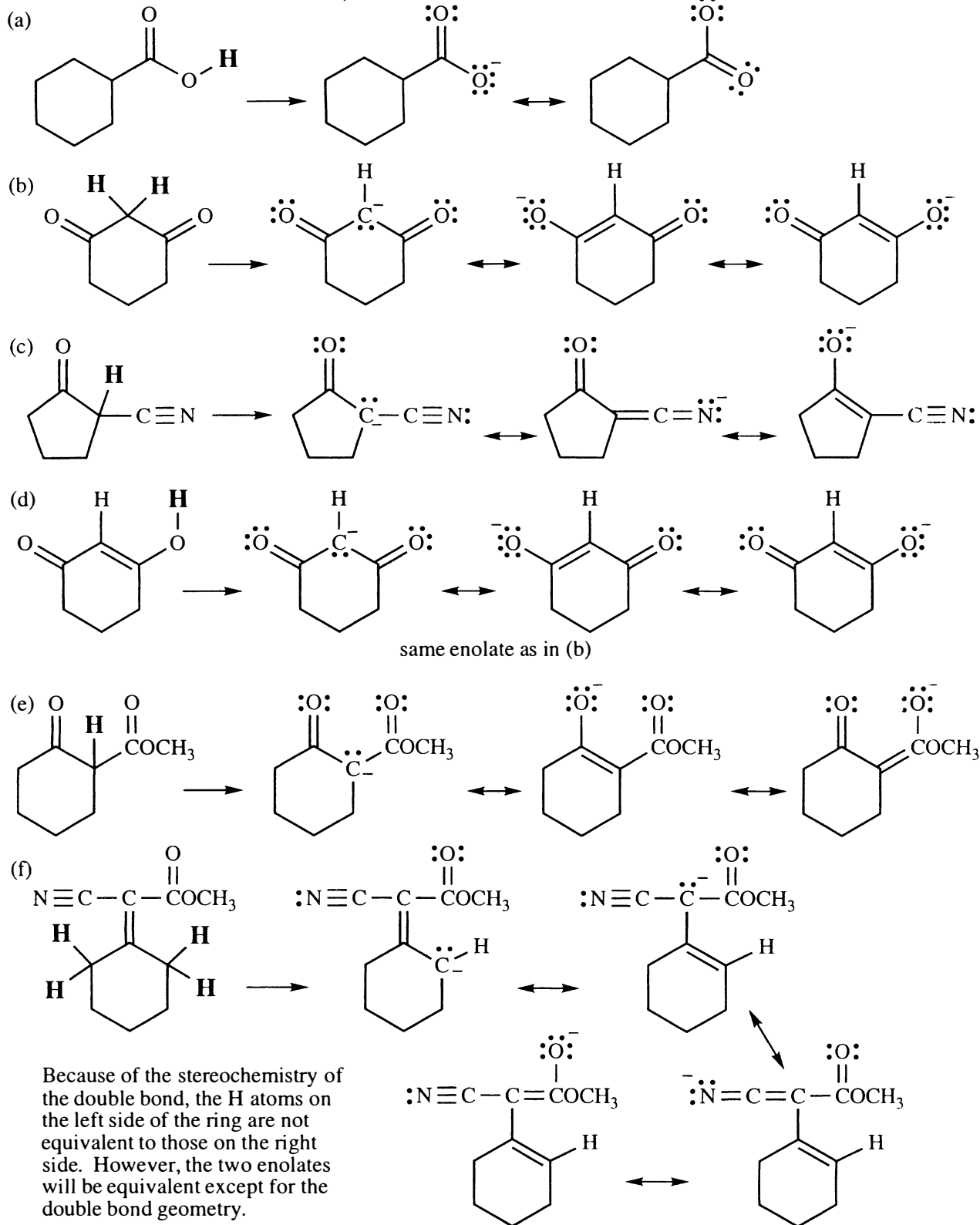


Michael addition forms a bond to the β' carbon:

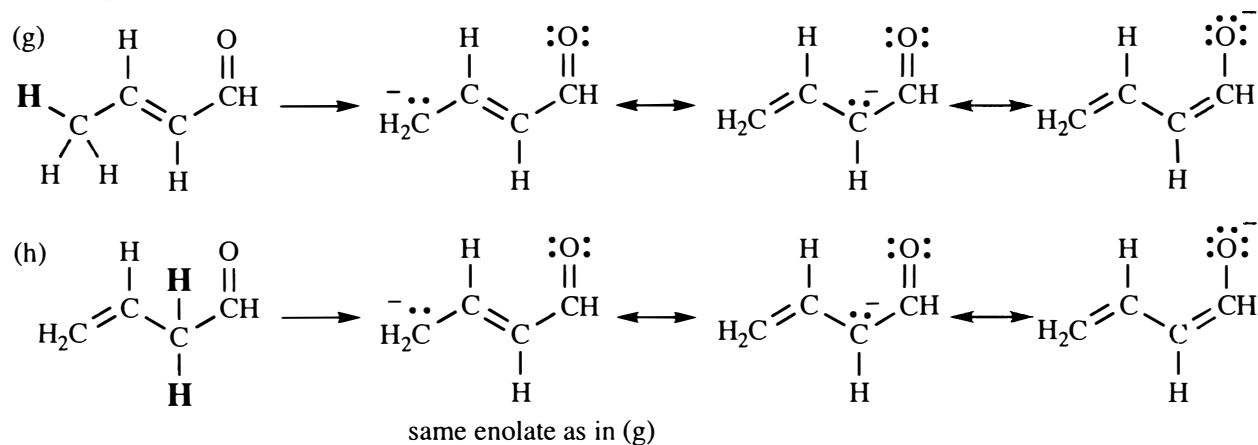


22-60 Please refer to solution 1-20, page 12 of this Solutions Manual.

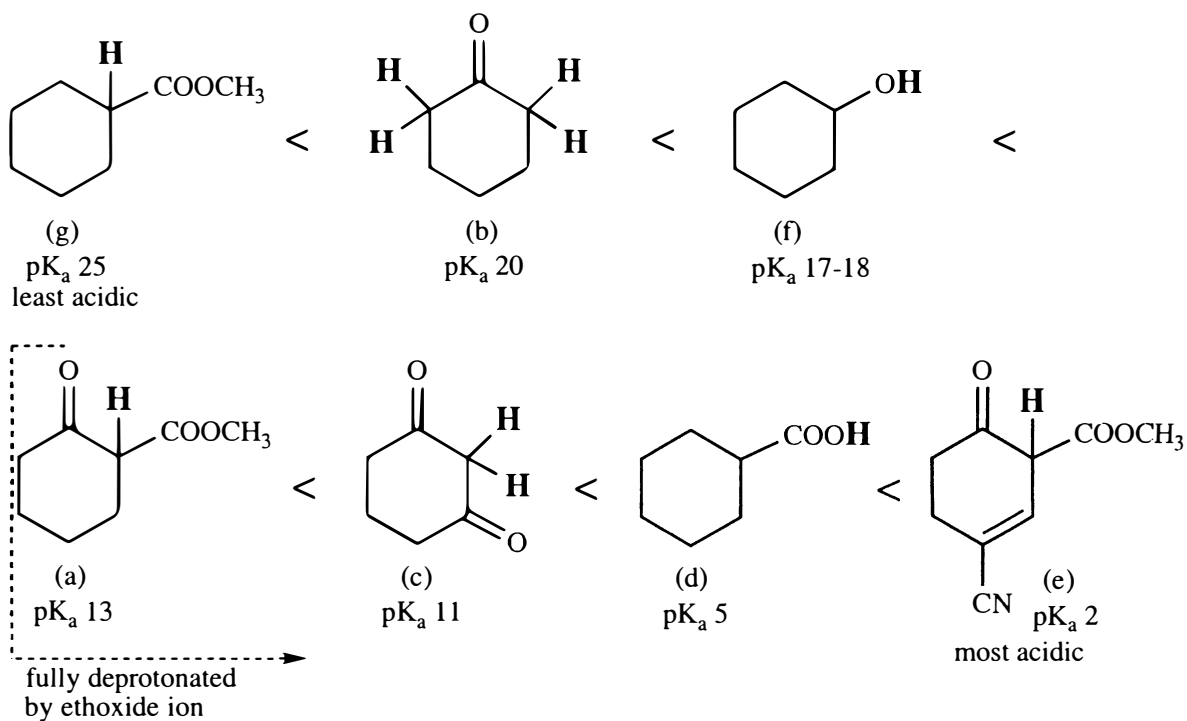
22-61 The most acidic hydrogens are shown in boldface. (See Appendix 2 for a review of acidity.) (Braces around resonance forms omitted here.)



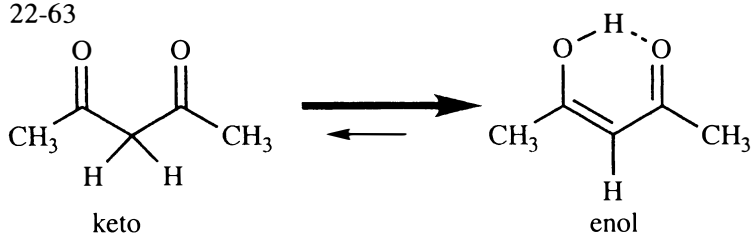
22-61 continued



22-62 In order of increasing acidity. The most acidic protons are shown in boldface. (The approximate pK_a values are shown for comparison.) See Appendix 2 for a review of acidity.

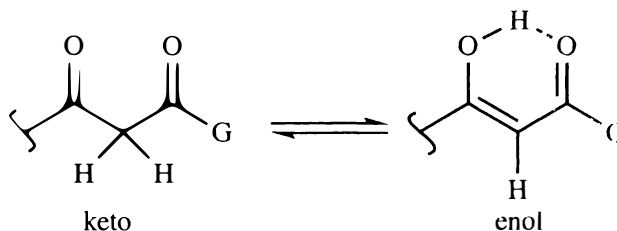


22-63

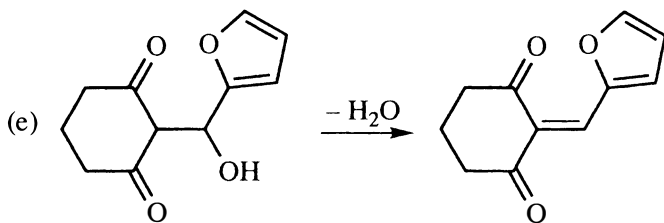
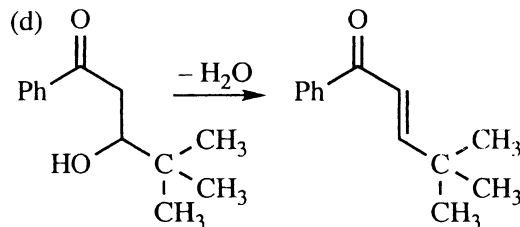
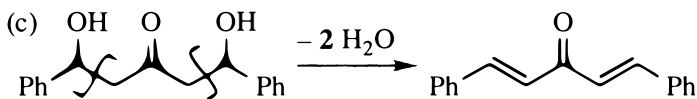
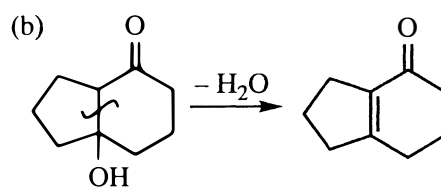
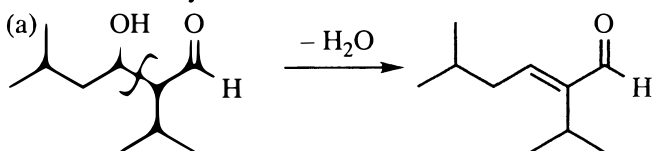


The enol form is stable because of the conjugation and because of intramolecular hydrogen-bonding in a six-membered ring.

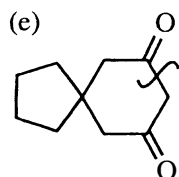
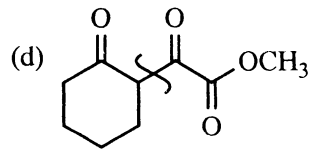
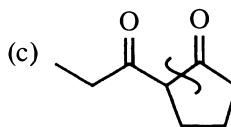
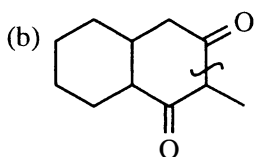
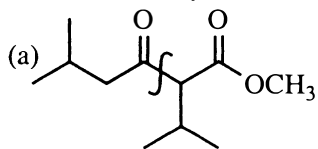
In dicarbonyl compounds in general, the weaker the electron-donating ability of the group G, the more it will exist in the enol form: aldehydes ($G = H$) are almost completely enolized, then ketones, esters, and finally amides which have virtually no enol content.

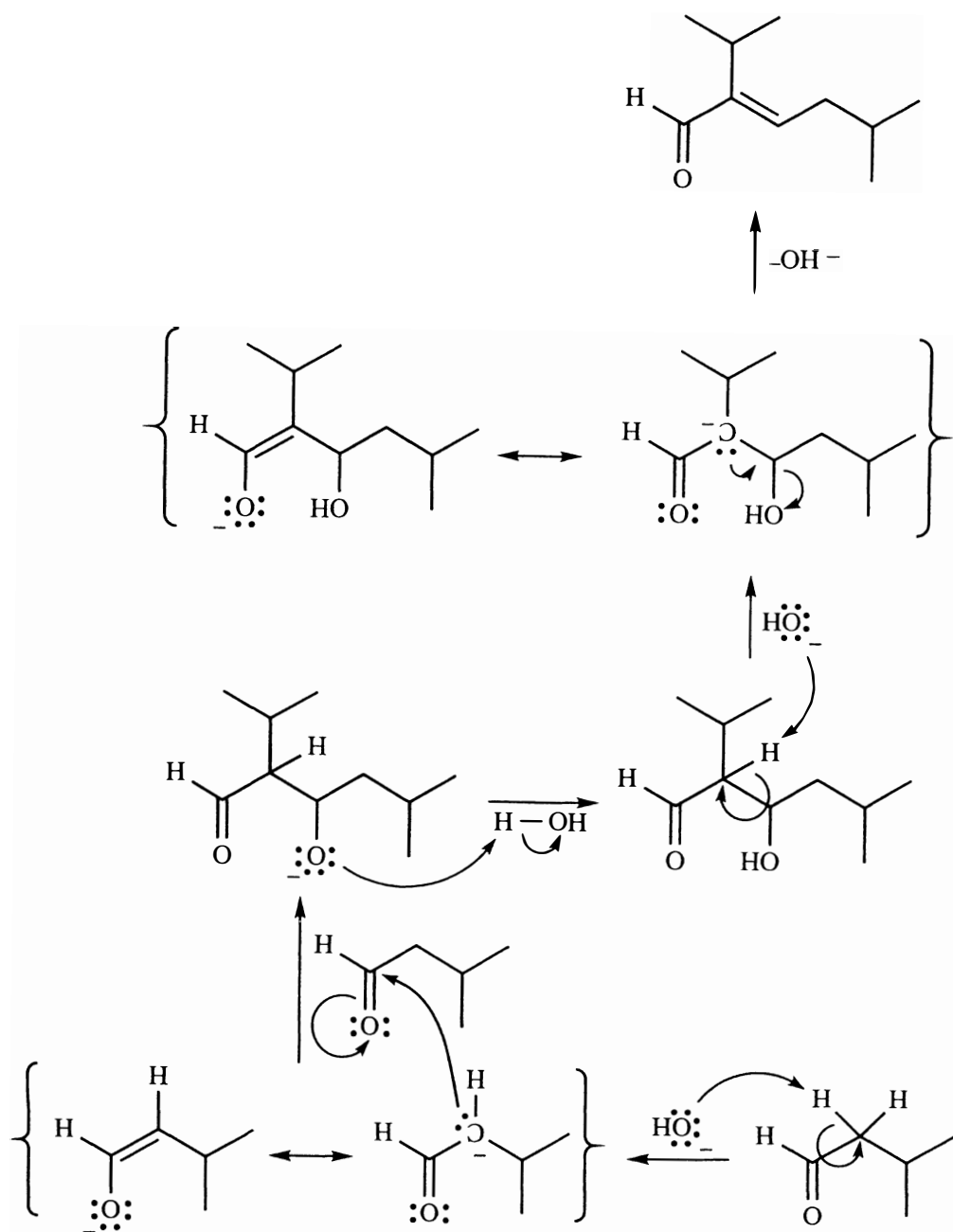


22-64 The wavy line lies across the bond formed in the aldol condensation.

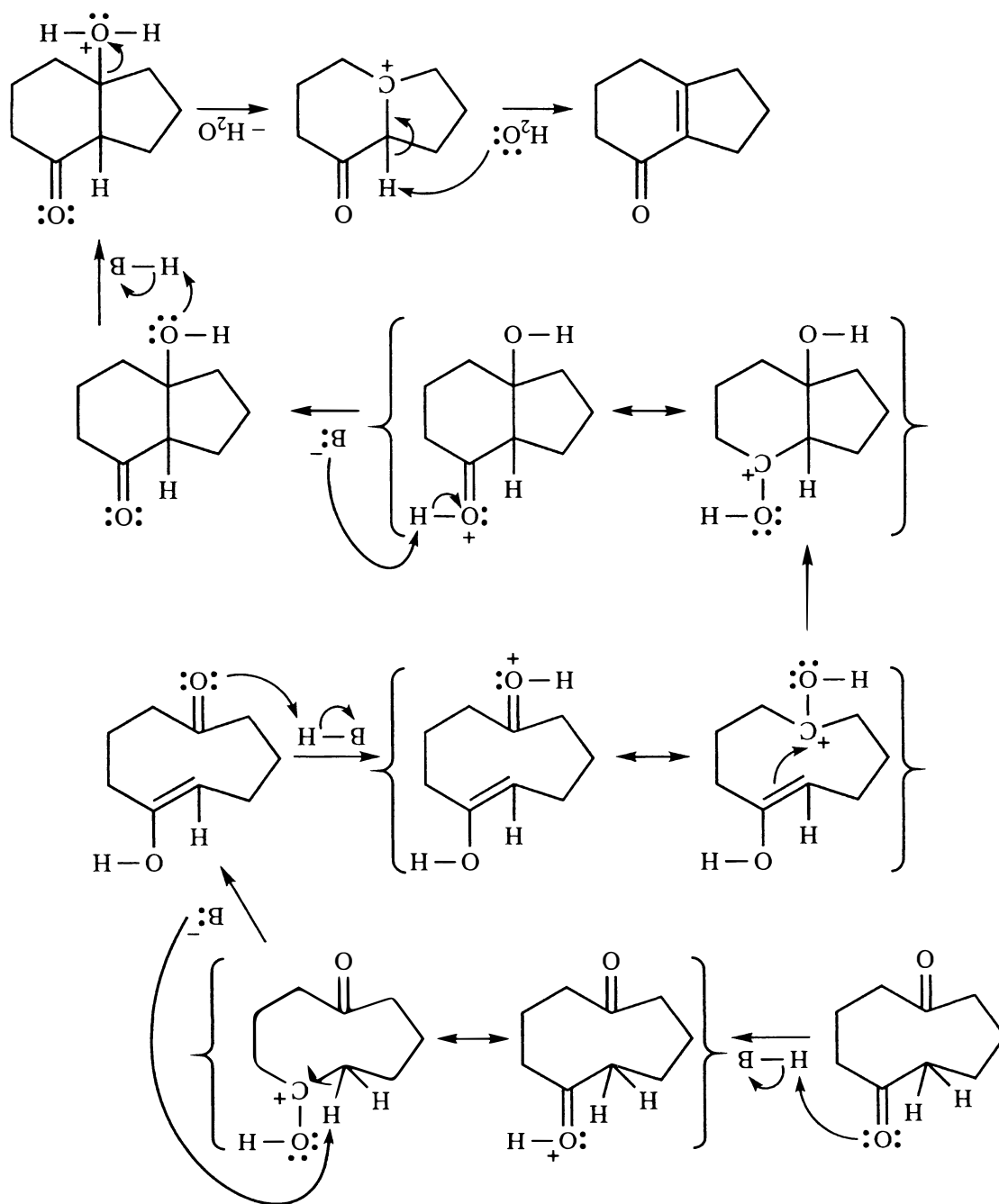


22-65 The wavy line lies across the bond formed in the Claisen condensation.





(a) mechanism of aldol condensation in problem 22-64(a)

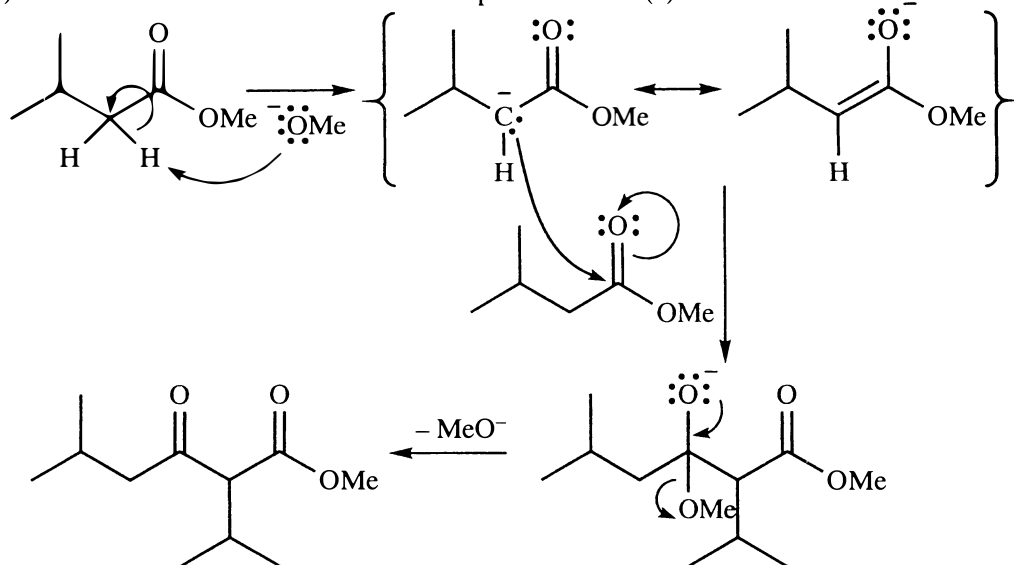


(b) mechanism of aldol condensation in problem 22-64(b)

22-66 continued

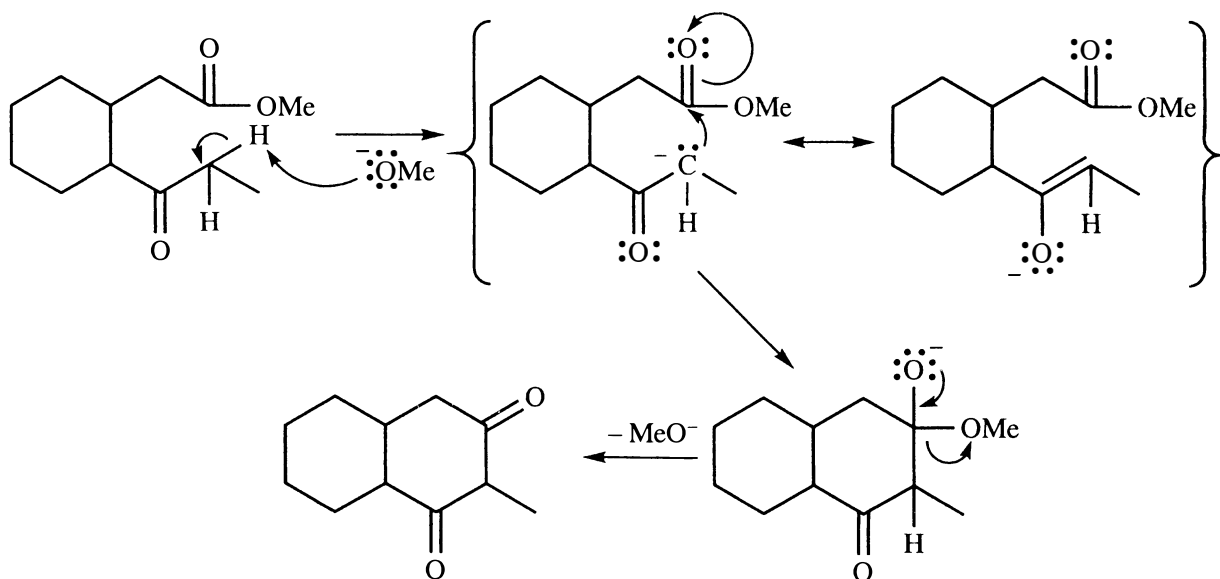
22-66 continued

(c) mechanism of Claisen condensation in problem 22-65(a)



(this product will be deprotonated by methoxide, but regenerated upon acidic workup)

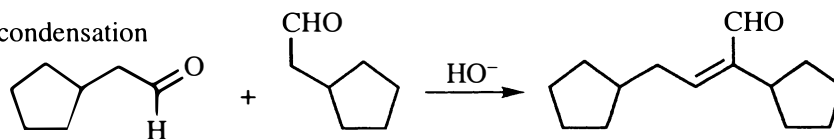
(d) mechanism of Claisen condensation in problem 22-65(b)



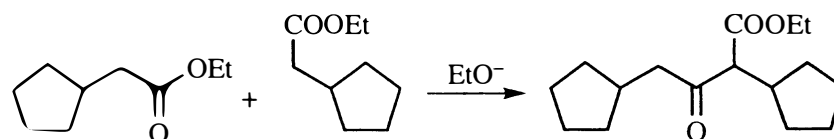
(this product will be deprotonated by methoxide, but regenerated upon acidic workup)

22-67 All products shown are after acidic workup.

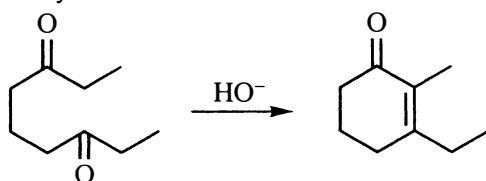
(a) aldol self-condensation



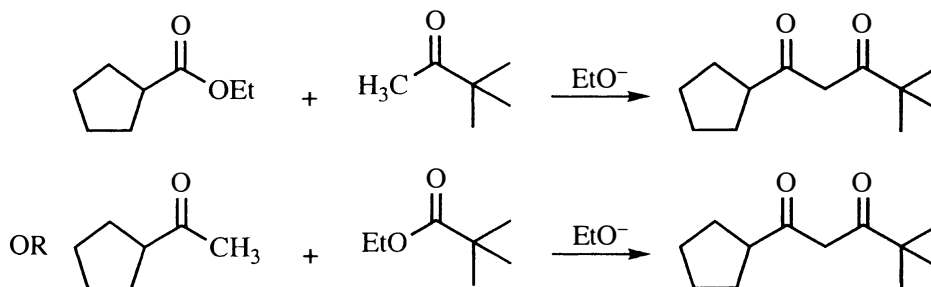
(b) Claisen self-condensation



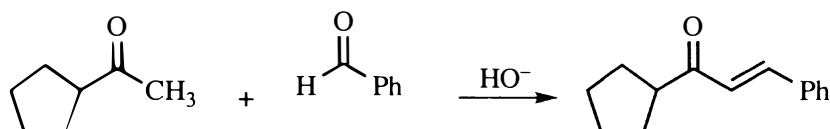
(c) aldol cyclization



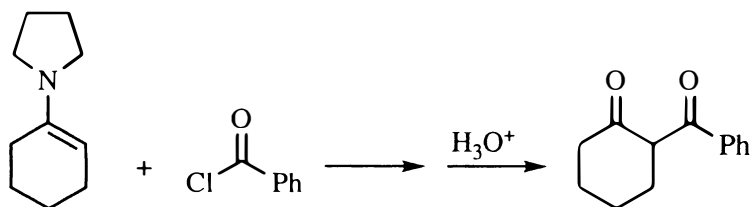
(d) mixed Claisen



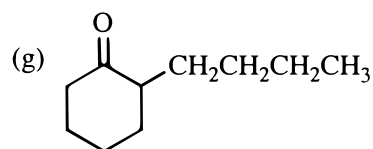
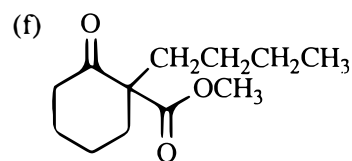
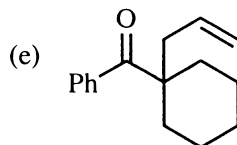
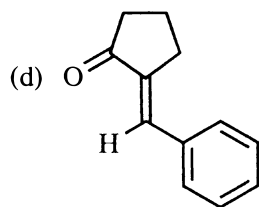
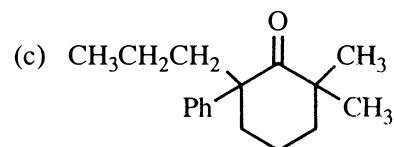
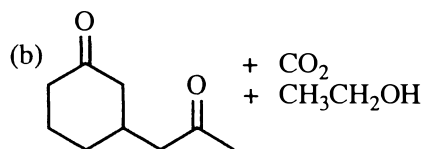
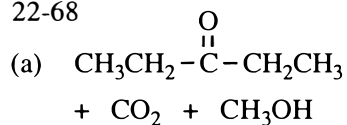
(e) mixed aldol



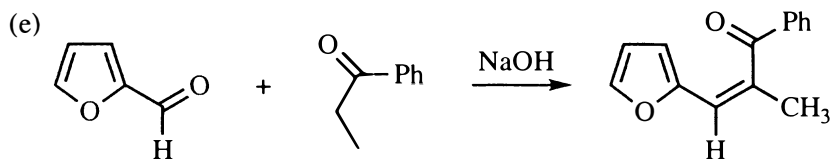
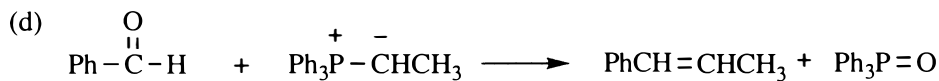
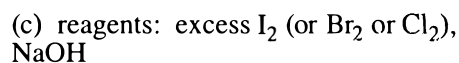
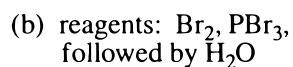
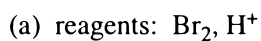
(f) enamine acylation—attempt at aldol would give self-condensation



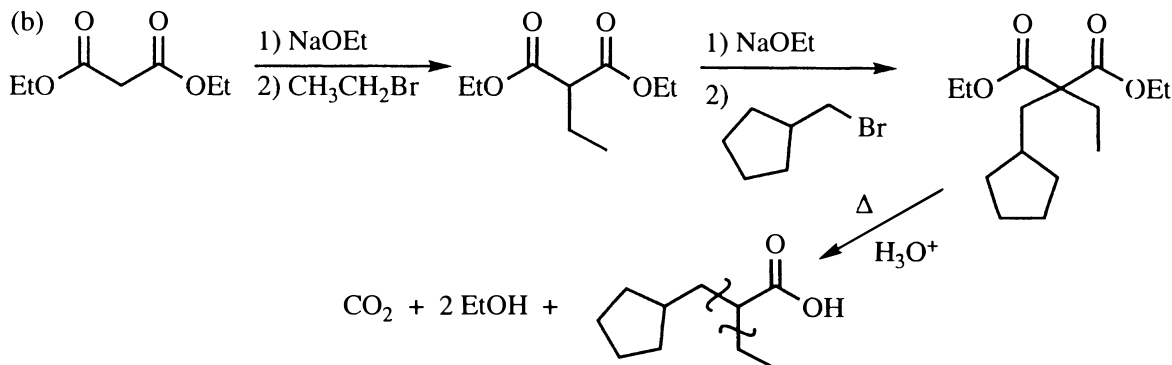
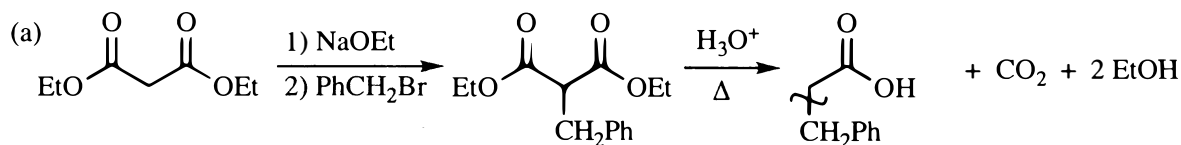
22-68



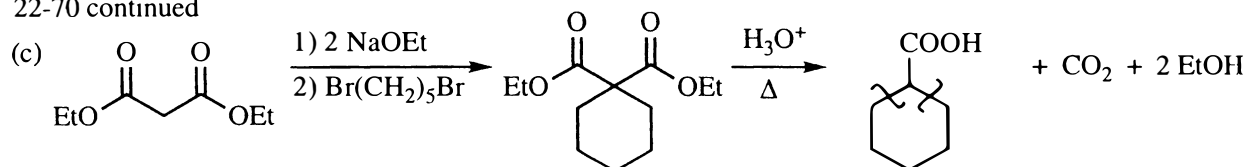
22-69



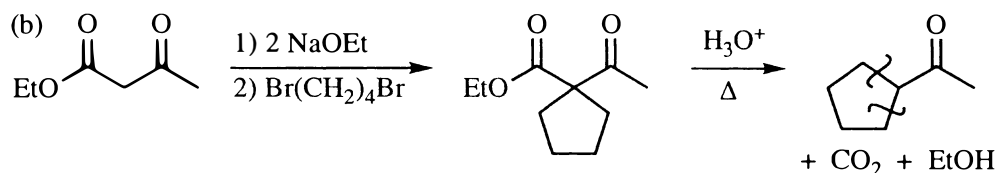
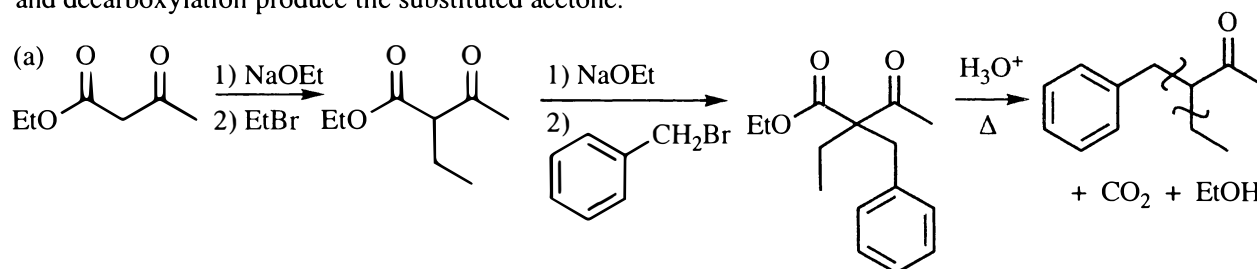
22-70 In the products, the wavy lines indicate the bonds that must be made by alkylation, before hydrolysis and decarboxylation produce the substituted acetic acid.



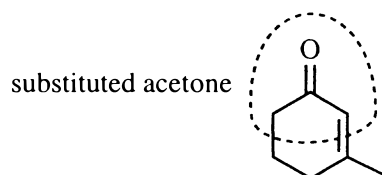
22-70 continued



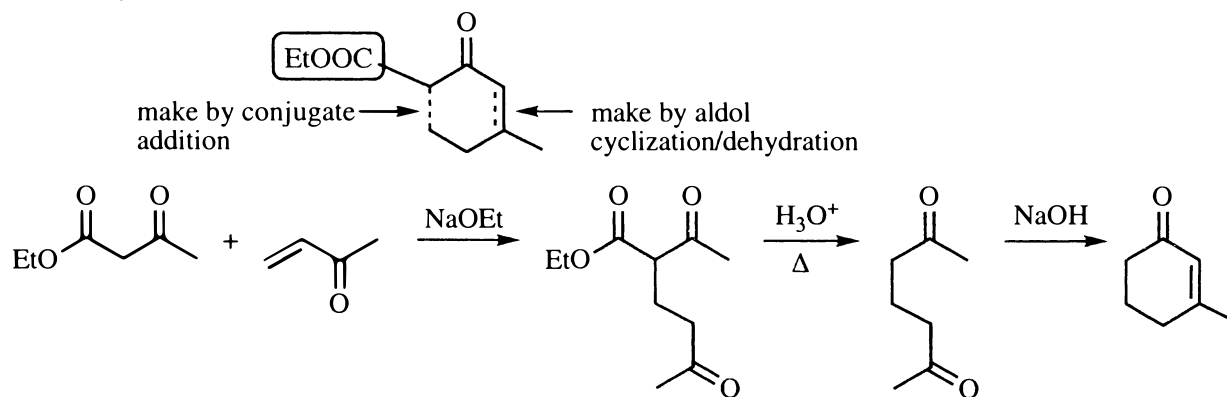
22-71 In the products, the wavy lines indicate the bonds that must be made by alkylation, before hydrolysis and decarboxylation produce the substituted acetone.



(c) The acetoacetic ester synthesis makes substituted acetone, so where is the acetone in this product?

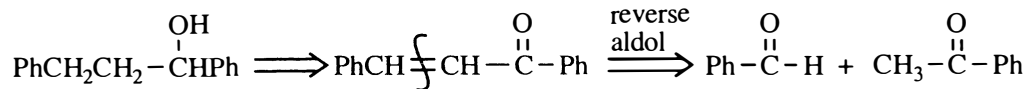


The single bond to this substituted acetone can be made by the acetoacetic ester synthesis. How can we make the α,β double bond? Aldol condensation!

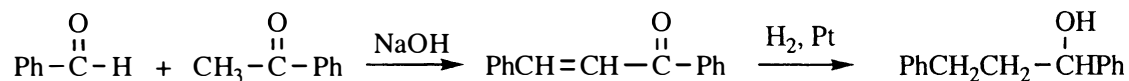


22-72 These compounds are made by aldol condensations followed by other reactions. The key is to find the skeleton made by the aldol.

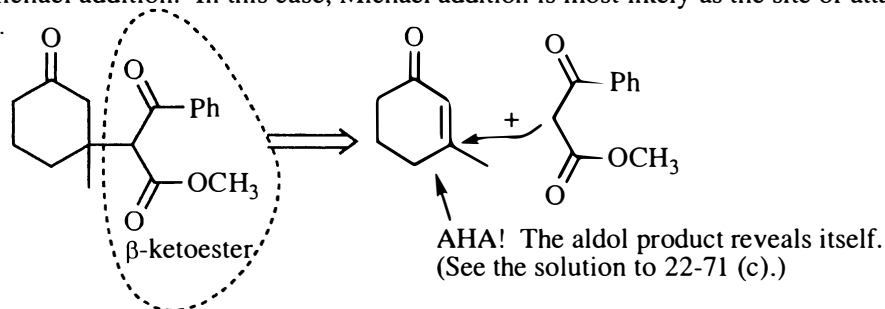
(a) Where is the possible α,β -unsaturated carbonyl in this skeleton?



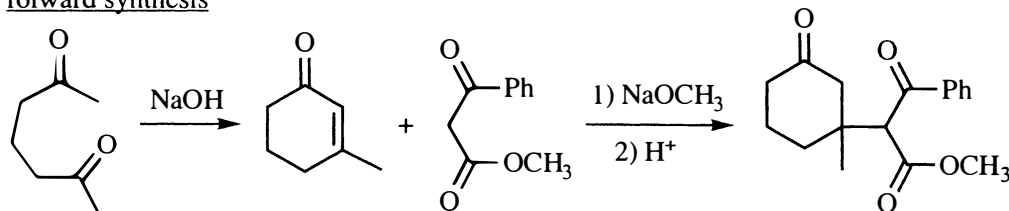
forward synthesis



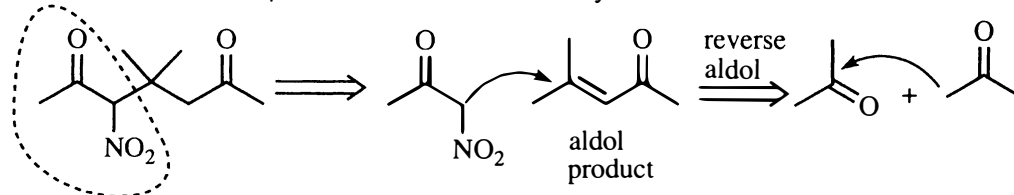
(b) The aldol skeleton is not immediately apparent in this formidable product. What can we see from it? Most obvious is the β -dicarbonyl (β -ketoester) which we know to be a good nucleophile, capable of substitution or Michael addition. In this case, Michael addition is most likely as the site of attack is β to another carbonyl.



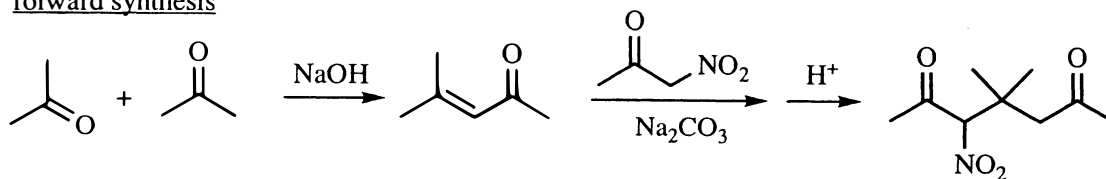
forward synthesis

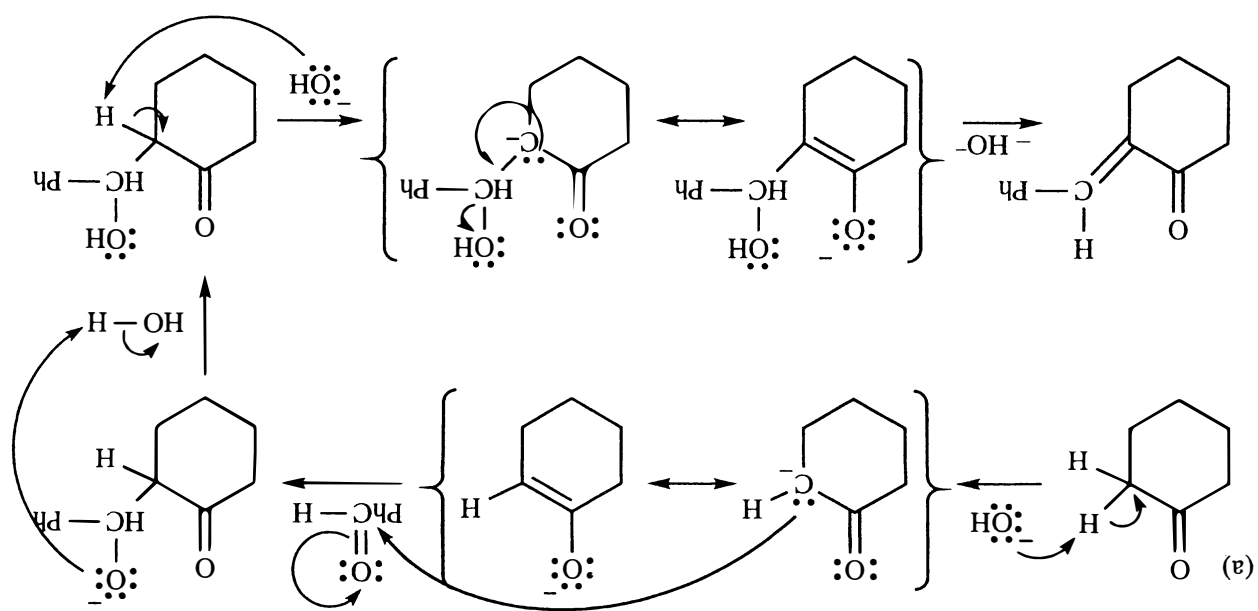
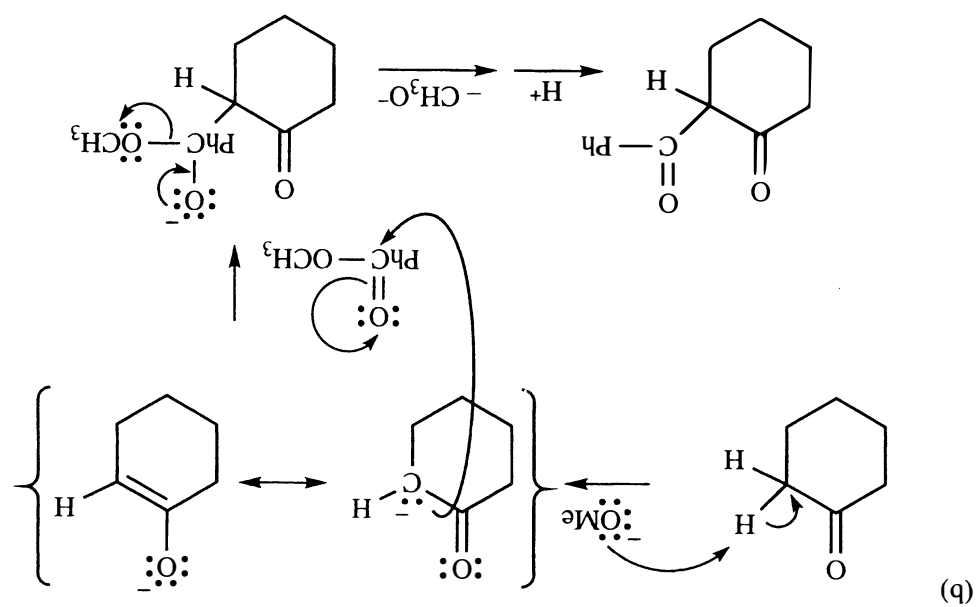


(c) The key in this product is the α -nitroketone, the equivalent of a β -dicarbonyl system, capable of doing Michael addition to the β -carbon of the other carbonyl.



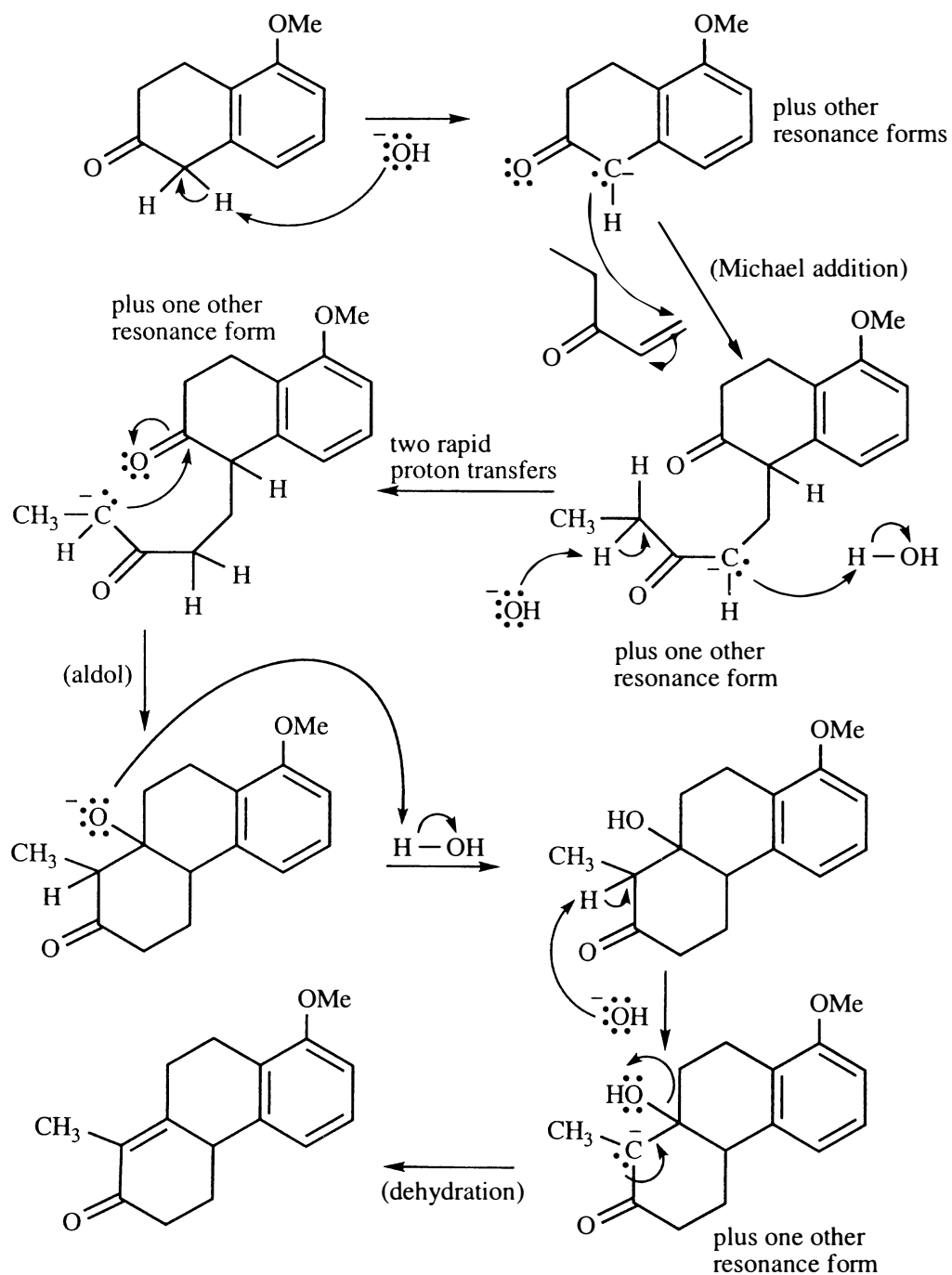
forward synthesis





22-73 continued

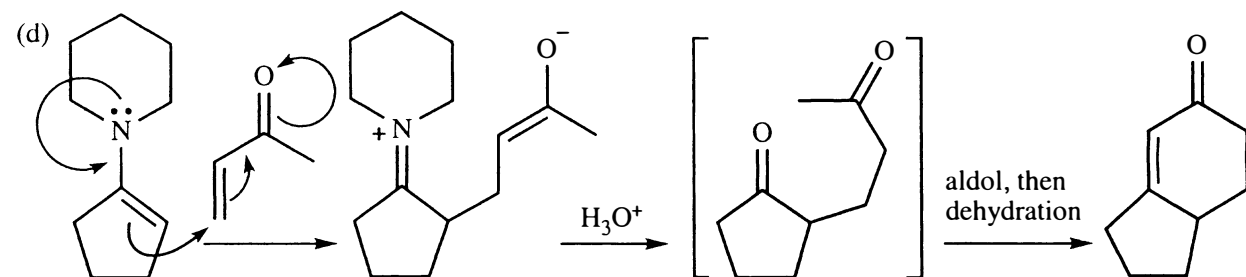
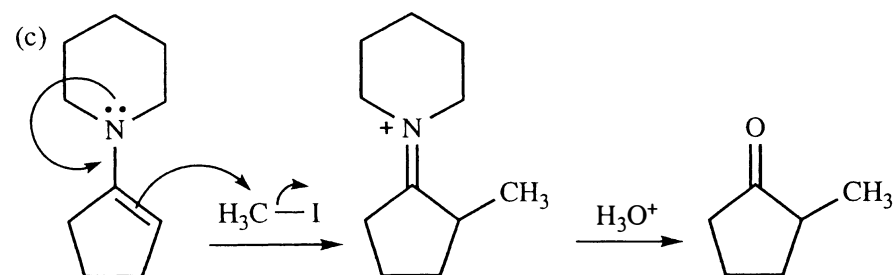
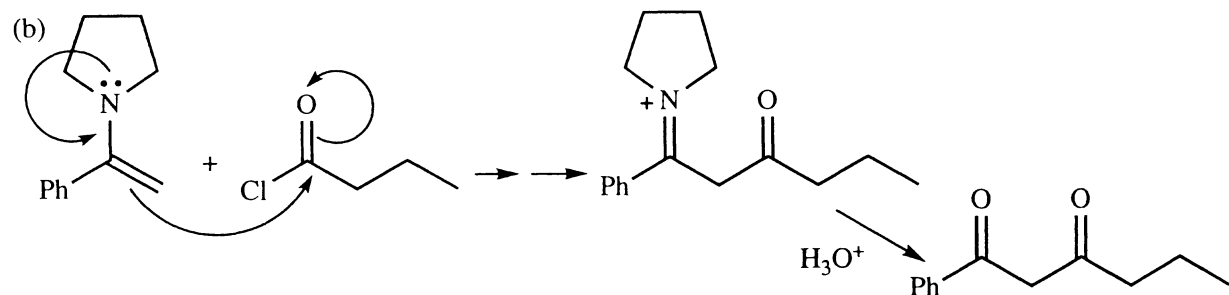
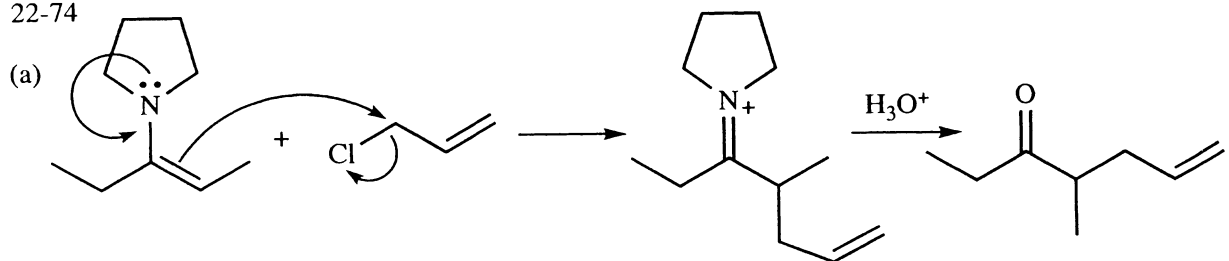
(c) Robinson annulations are explained most easily by remembering that the first step is a Michael addition, followed by aldol cyclization with dehydration.



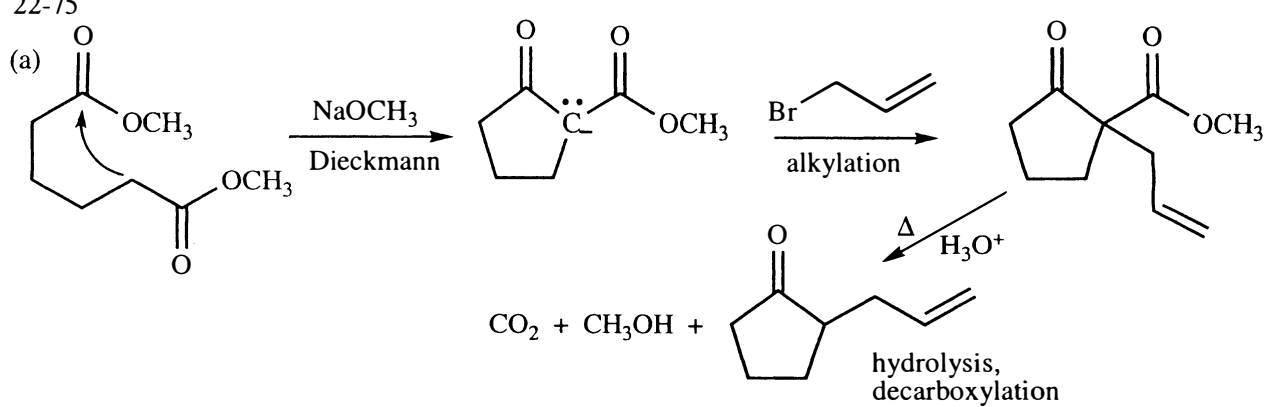
(d)



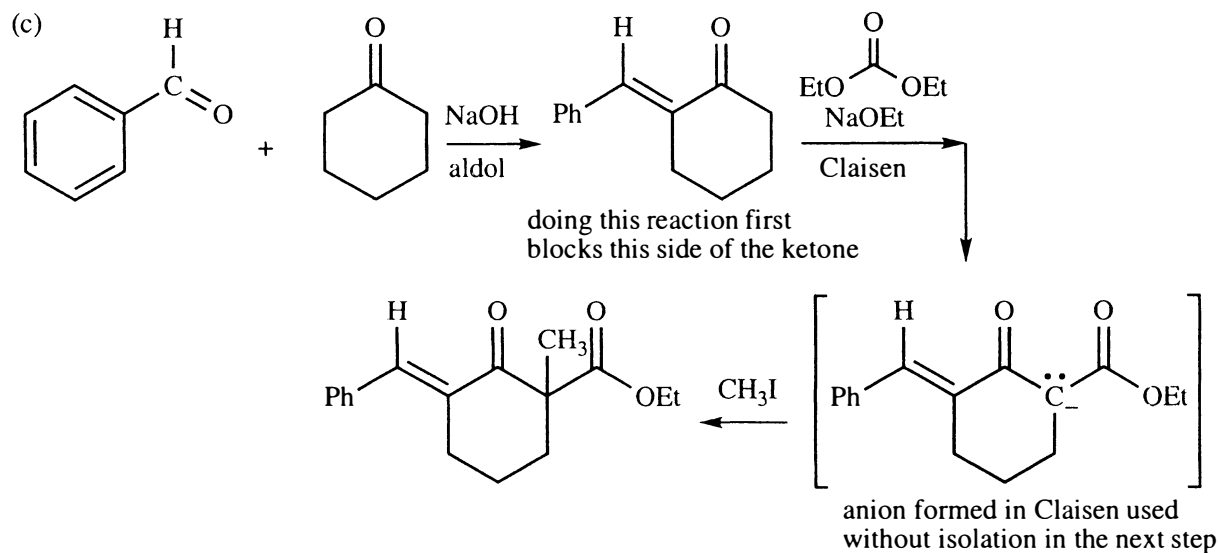
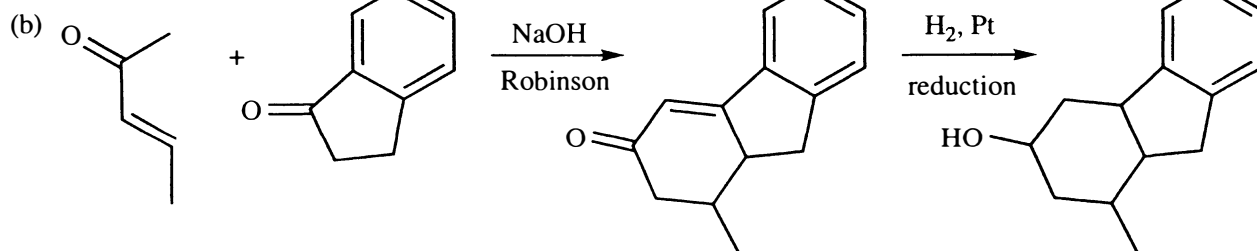
22-74



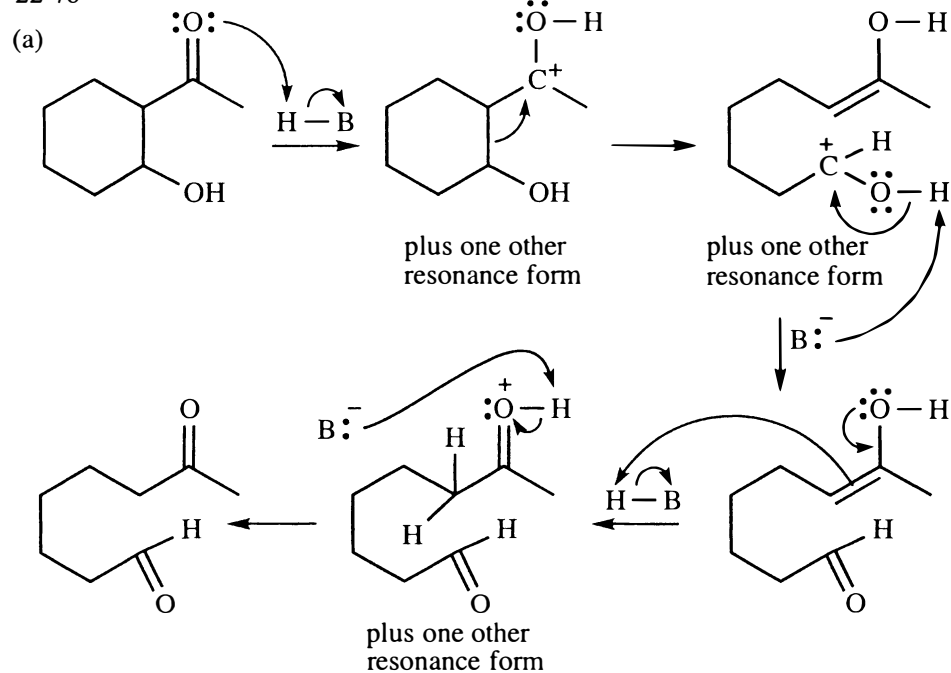
22-75



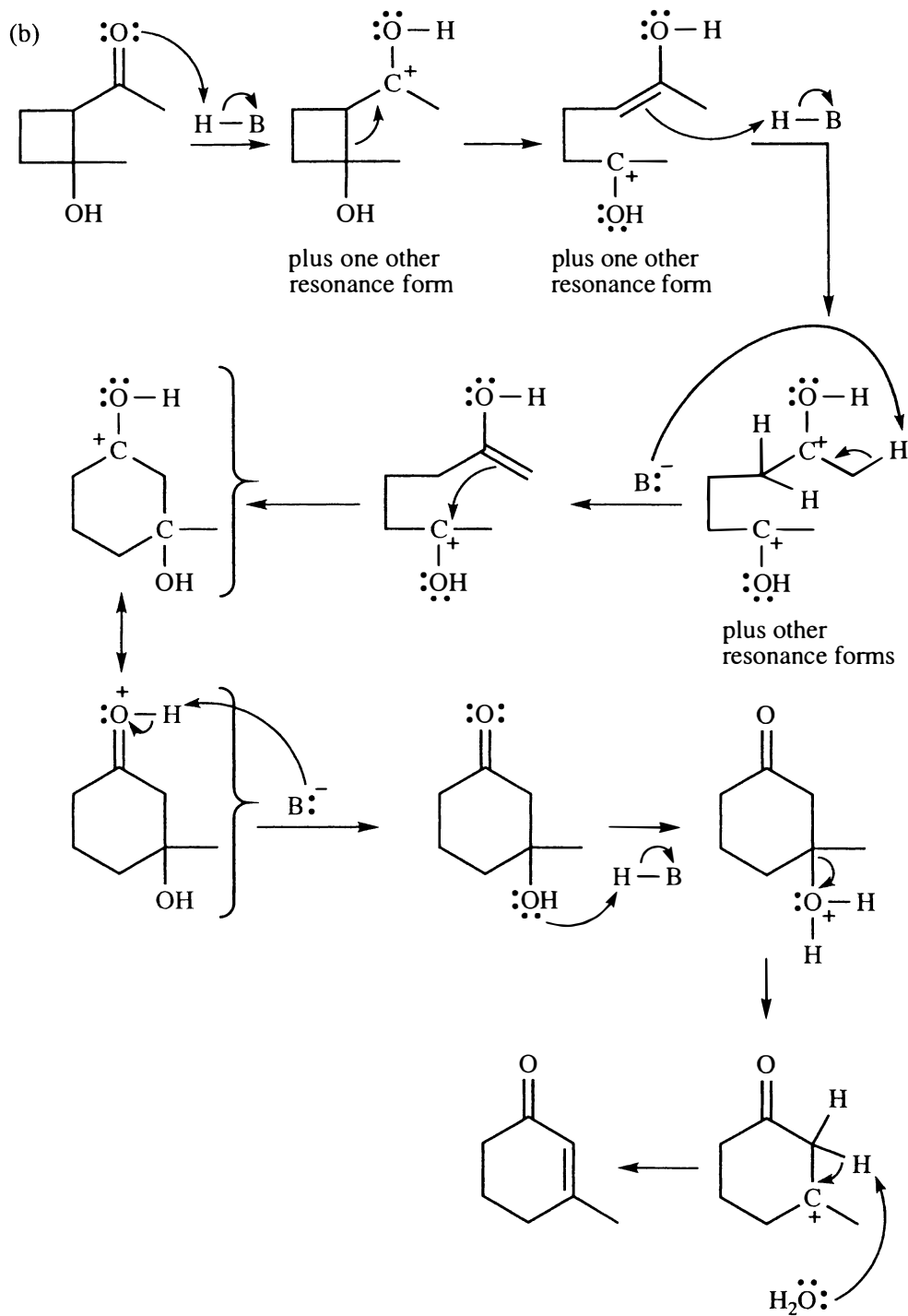
22-75 continued



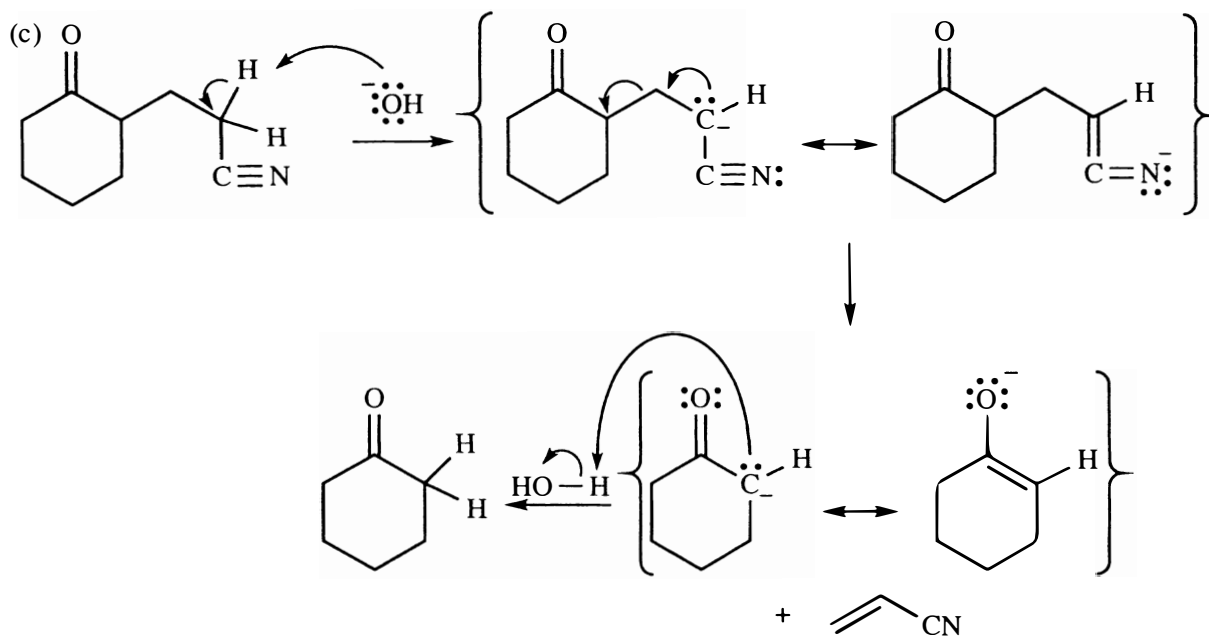
22-76



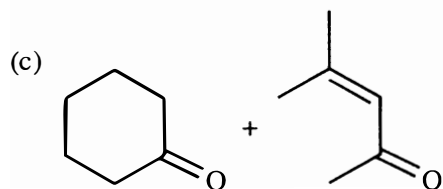
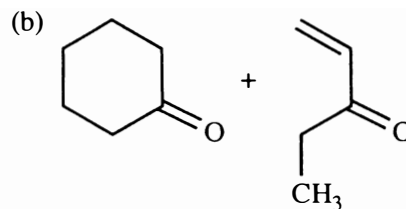
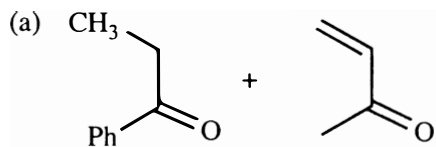
22-76 continued



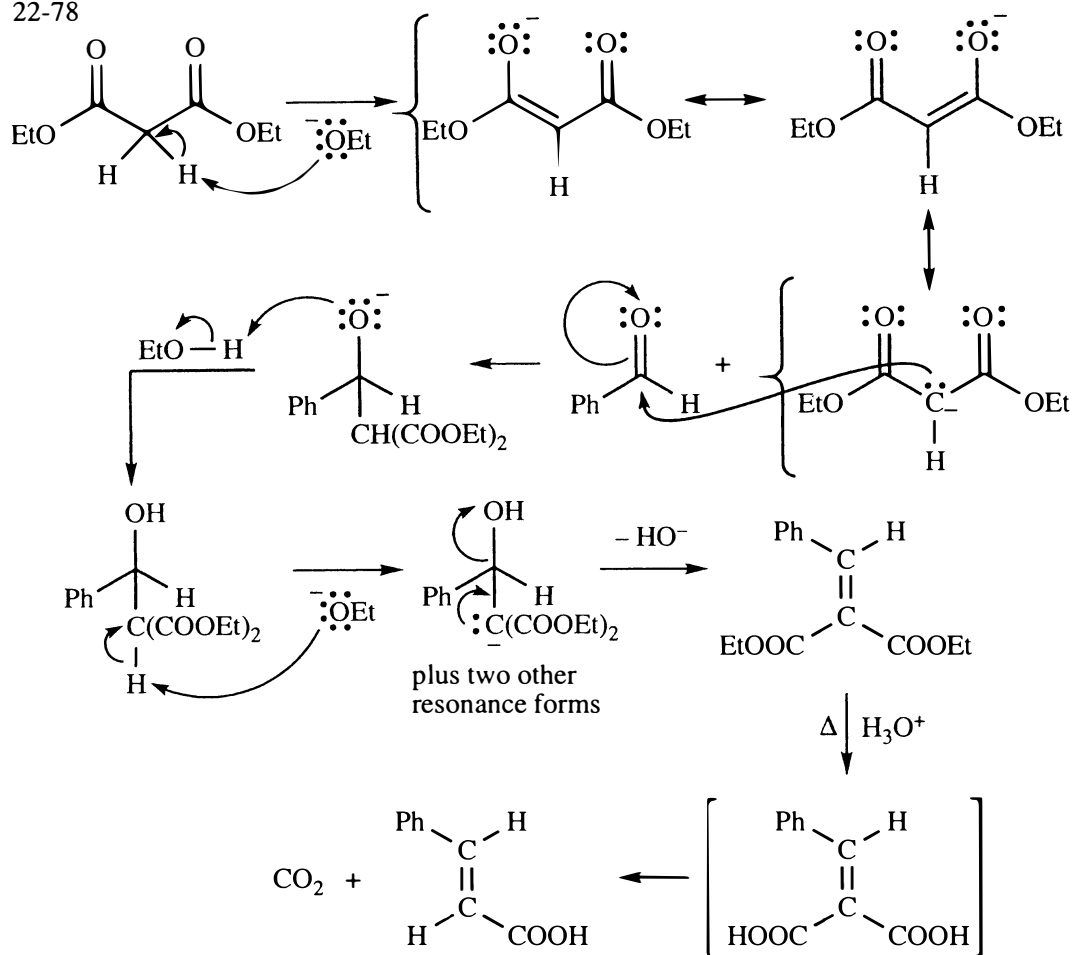
22-76 continued



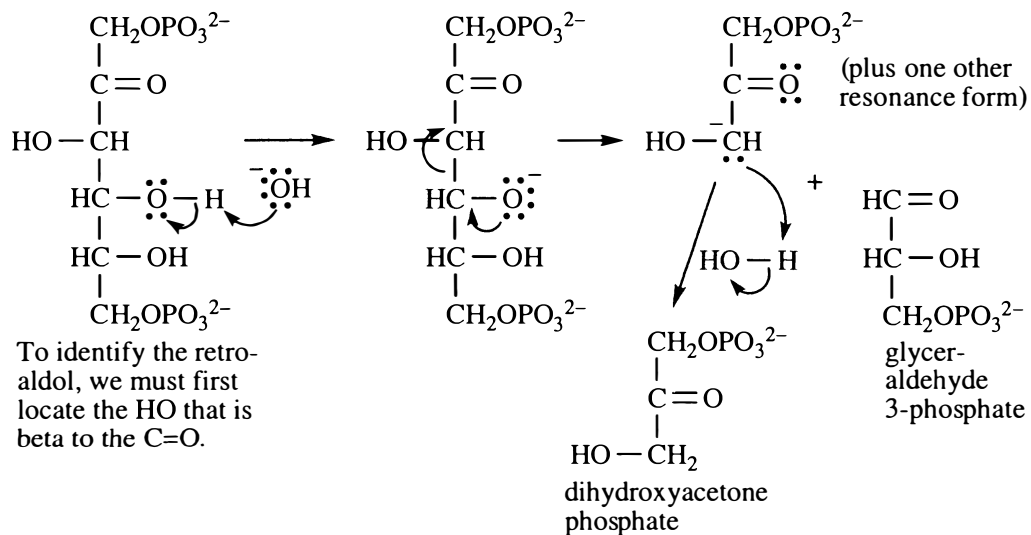
22-77 All of these Robinson annulations are catalyzed by NaOH.



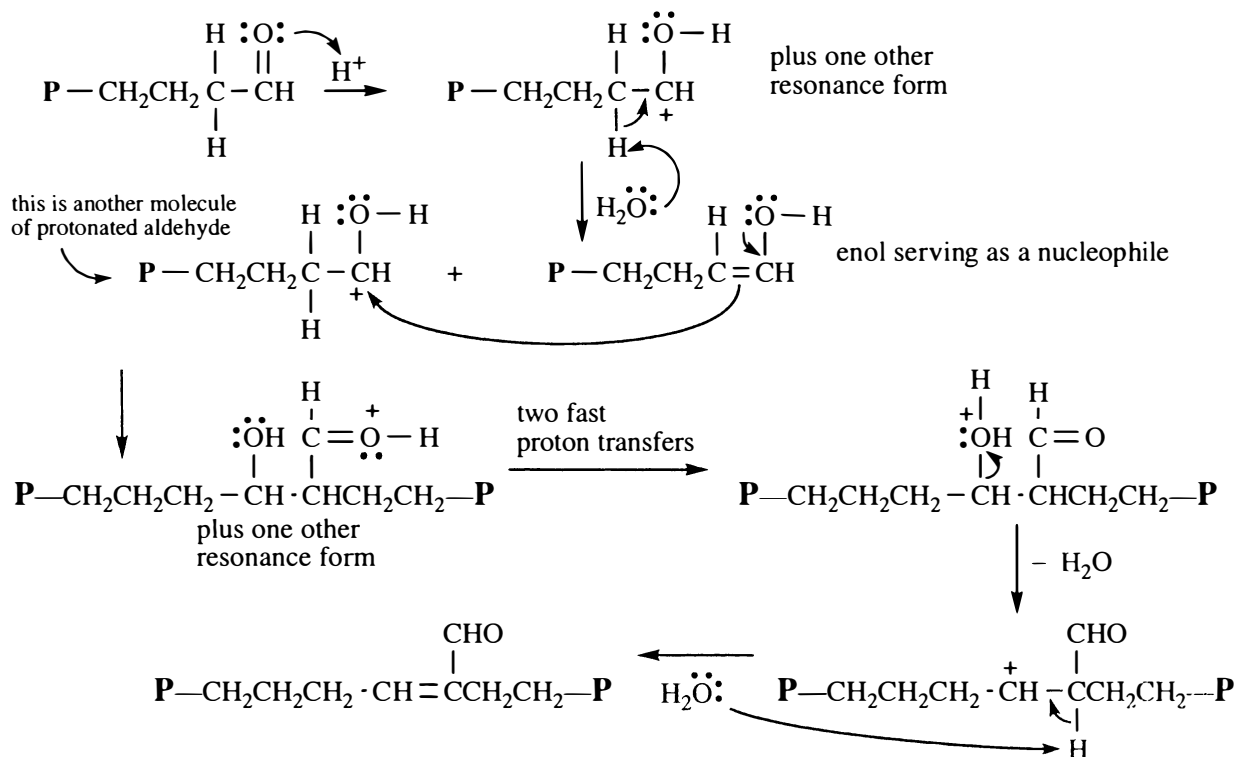
22-78



22-79

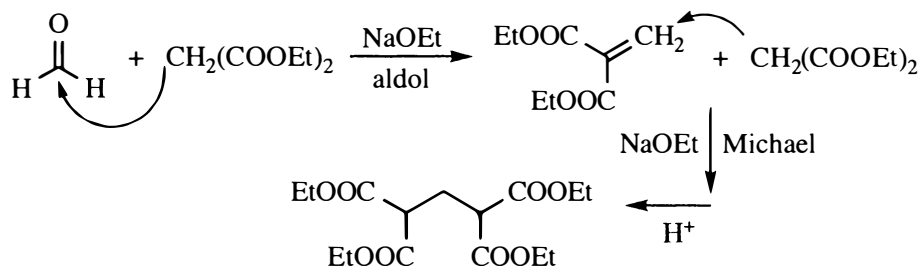


22-80 This is an aldol condensation. **P** stands for a protein chain in this problem.

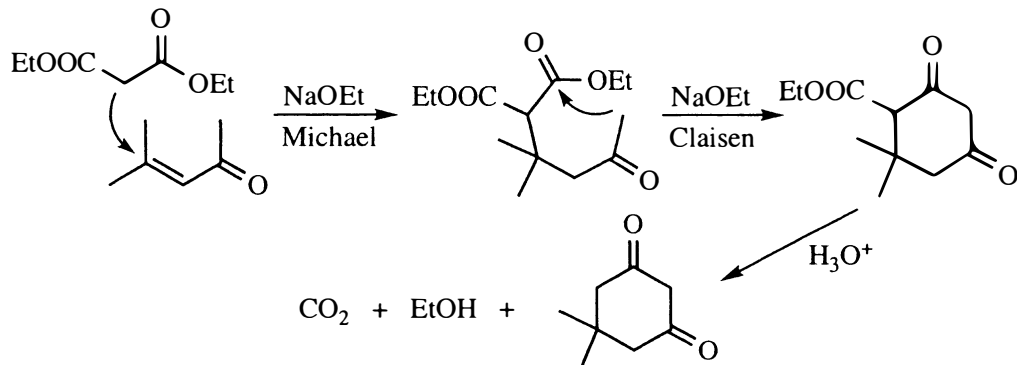


22-81

(a) aldol followed by Michael

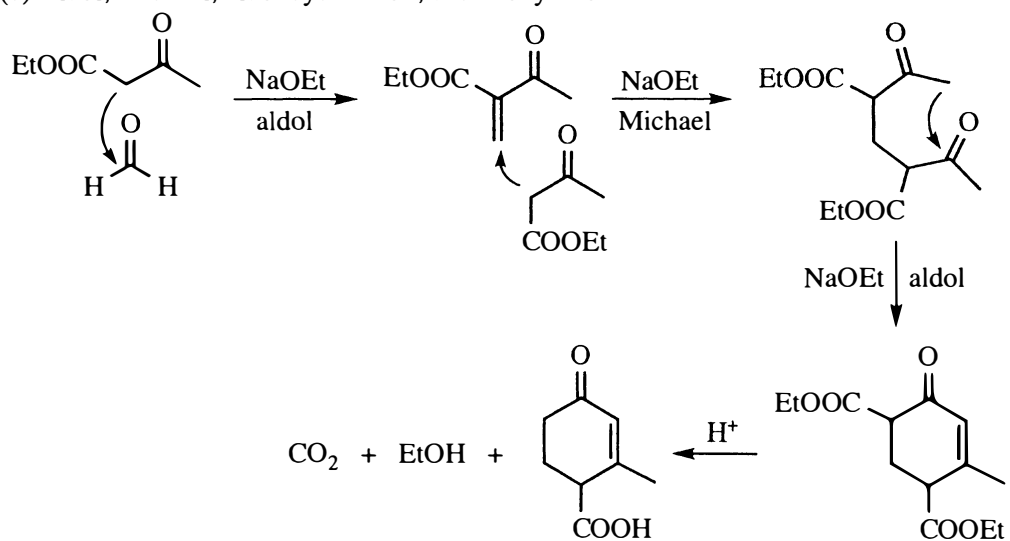


(b) Michael followed by Claisen condensation; hydrolysis and decarboxylation



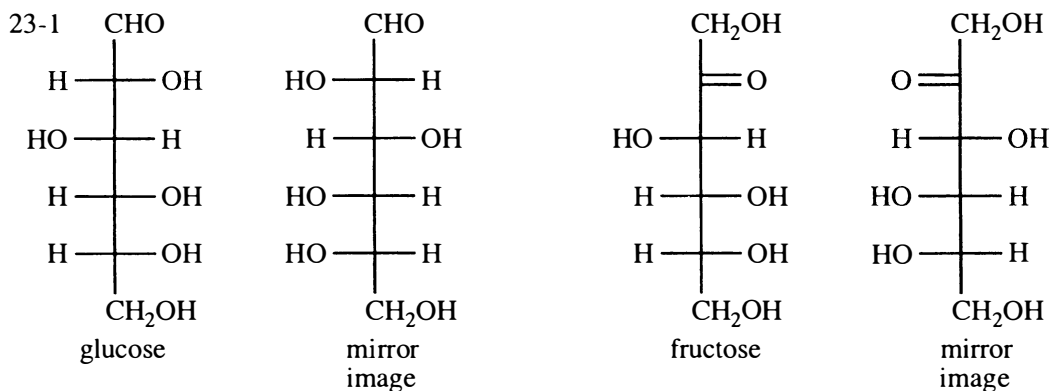
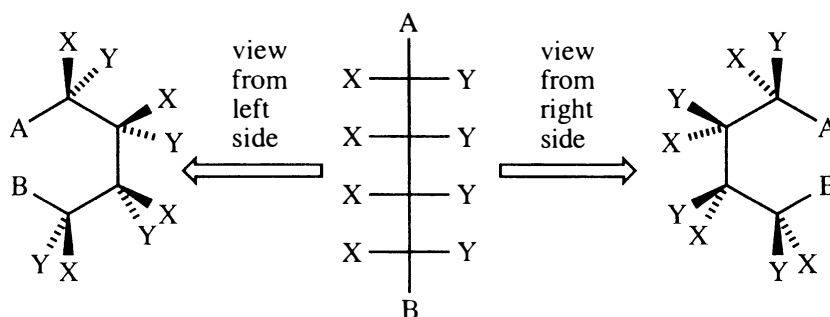
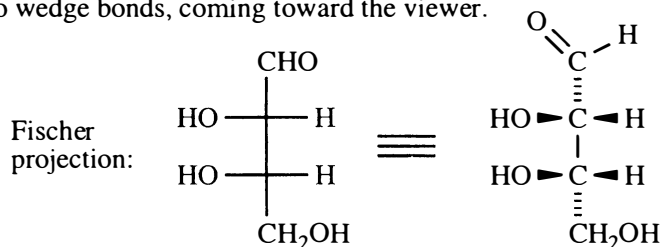
22-81 continued

(c) aldol, Michael, aldol cyclization, decarboxylation

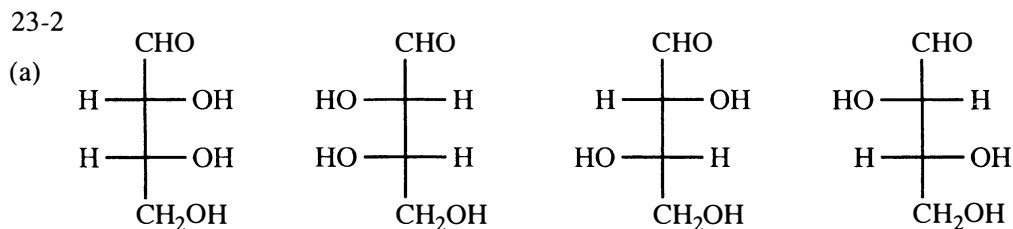


CHAPTER 23—CARBOHYDRATES AND NUCLEIC ACIDS

Reminder about Fischer projections, first introduced in Chapter 5, section 5-10: vertical bonds are equivalent to dashed bonds, going behind the plane of the paper, and horizontal bonds are equivalent to wedge bonds, coming toward the viewer.

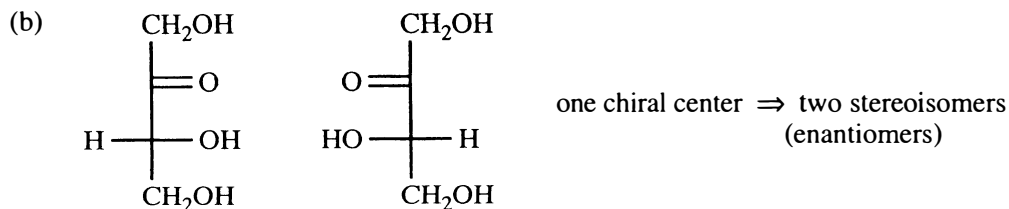


All four of these compounds are chiral and optically active.

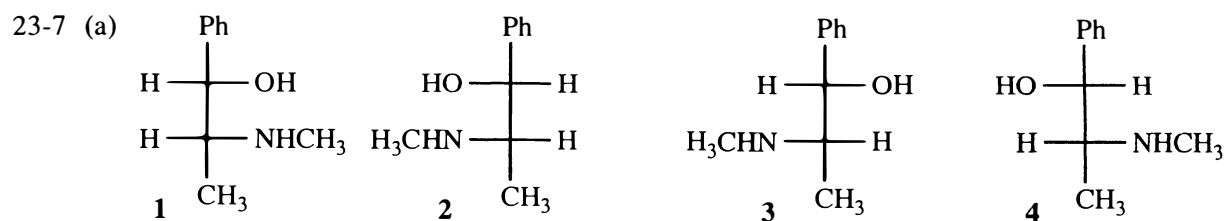
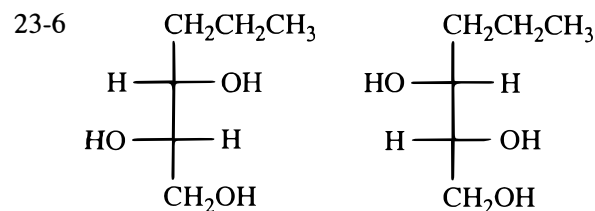
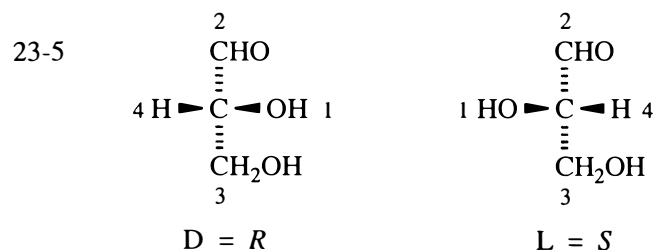
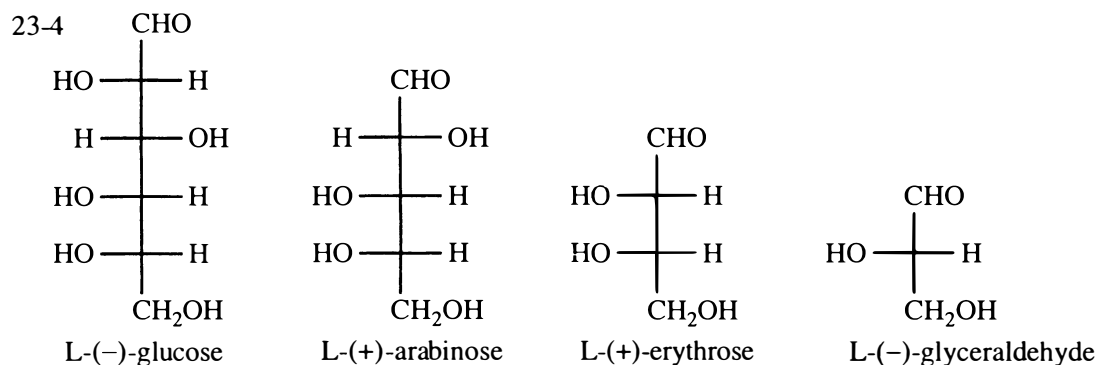
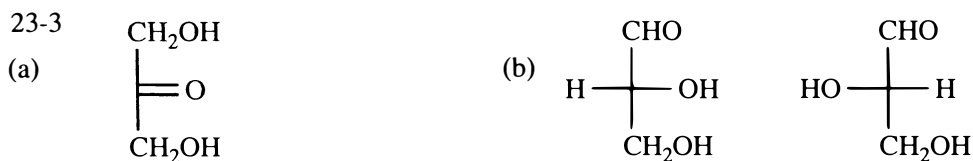


two asymmetric carbons $\Rightarrow$ four stereoisomers (two pairs of enantiomers) if none are meso

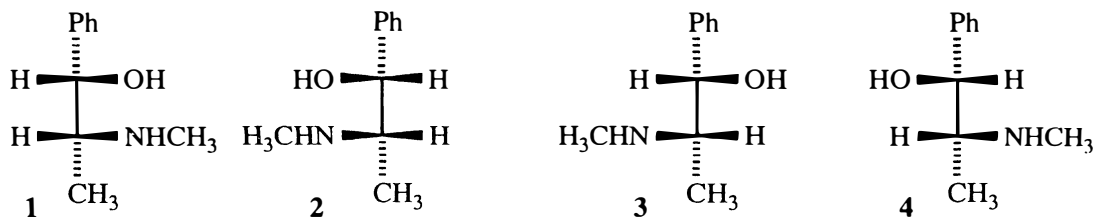
23-2 continued



(c) An aldohexose has four chiral carbons and sixteen stereoisomers. A ketohexose has three chiral carbons and eight stereoisomers.



23-7 (a) continued

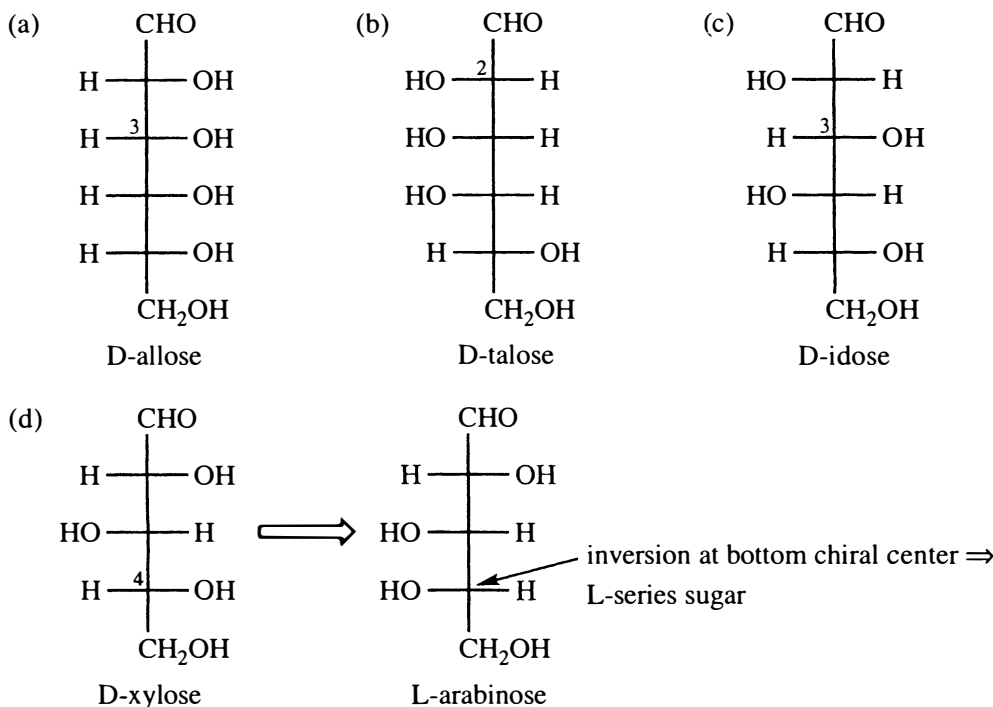


(b) Ephedrine is the *erythro* diastereomer, represented by structures **1** and **2**. Structures **3** and **4** represent pseudoephedrine, the *threo* diastereomer.

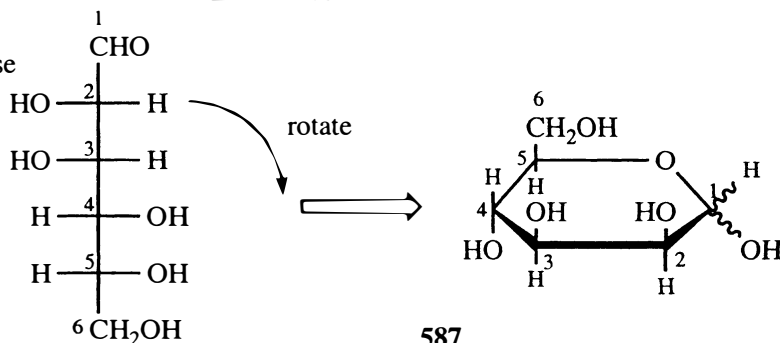
(c) The Fischer-Rosanoff convention assigns D and L to the configuration of the asymmetric carbon at the bottom of the Fischer projection. Structure **1** is D-ephedrine; structure **2** is L-ephedrine; structure **3** is L-pseudoephedrine; and structure **4** is D-pseudoephedrine.

(d) It is not possible to determine which is the (+) or (−) isomer of any compound just by looking at the structure. The only compound that has a direct correlation between the direction of optical rotation and its D or L designation is glyceraldehyde, about which the D and L system was designed. For all other compounds, optical rotation can only be determined by measurement in a polarimeter.

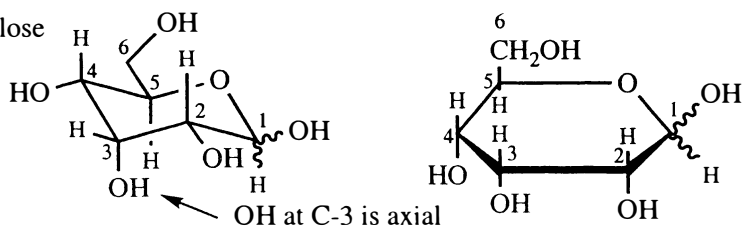
23-8



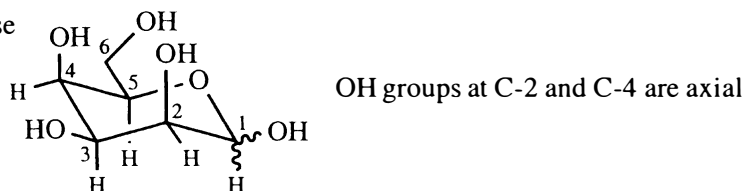
23-9 D-mannose



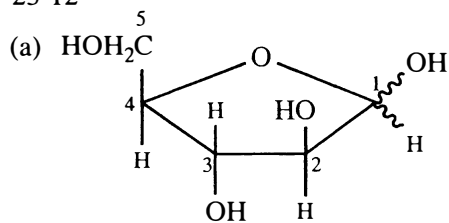
23-10 D-allose



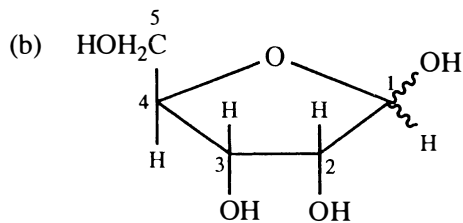
23-11 D-talopyranose



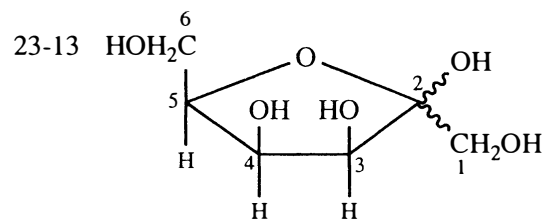
23-12



D-arabinofuranose

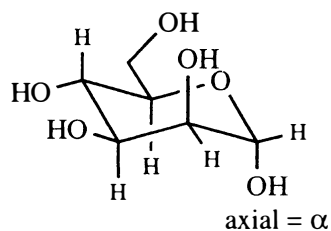


D-ribofuranose

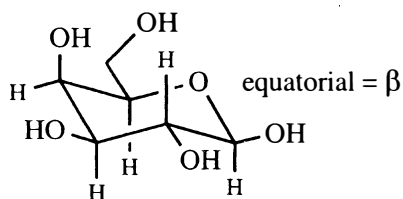


23-14

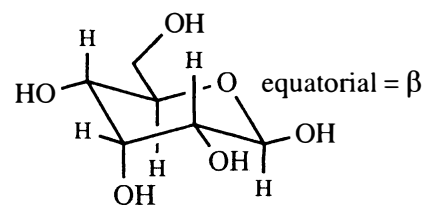
(a) α -D-mannopyranose



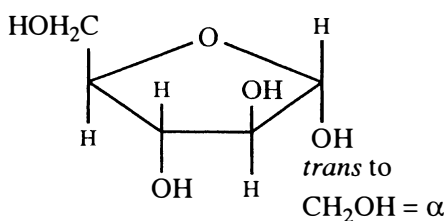
(b) β -D-galactopyranose



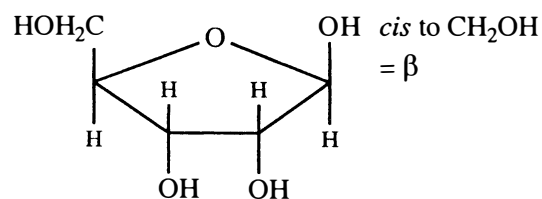
(c) β -D-allopyranose



(d) α -D-arabinofuranose



(e) β -D-ribofuranose



23-15 a = fraction of galactose as the α anomer; b = fraction of galactose as the β anomer

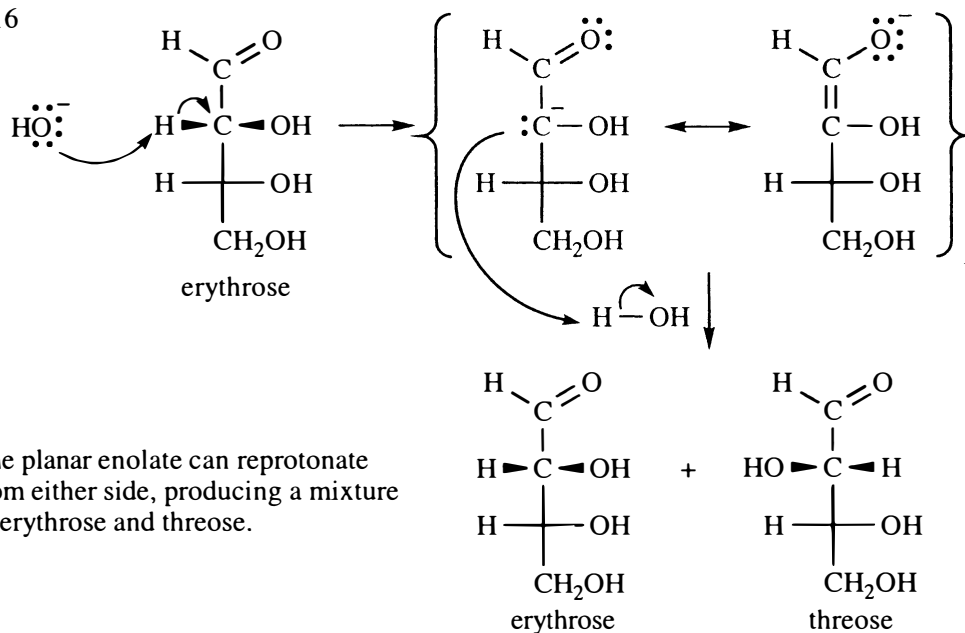
$$a(+150.7^\circ) + b(+52.8^\circ) = +80.2^\circ$$

$$a + b = 1; \quad b = 1 - a$$

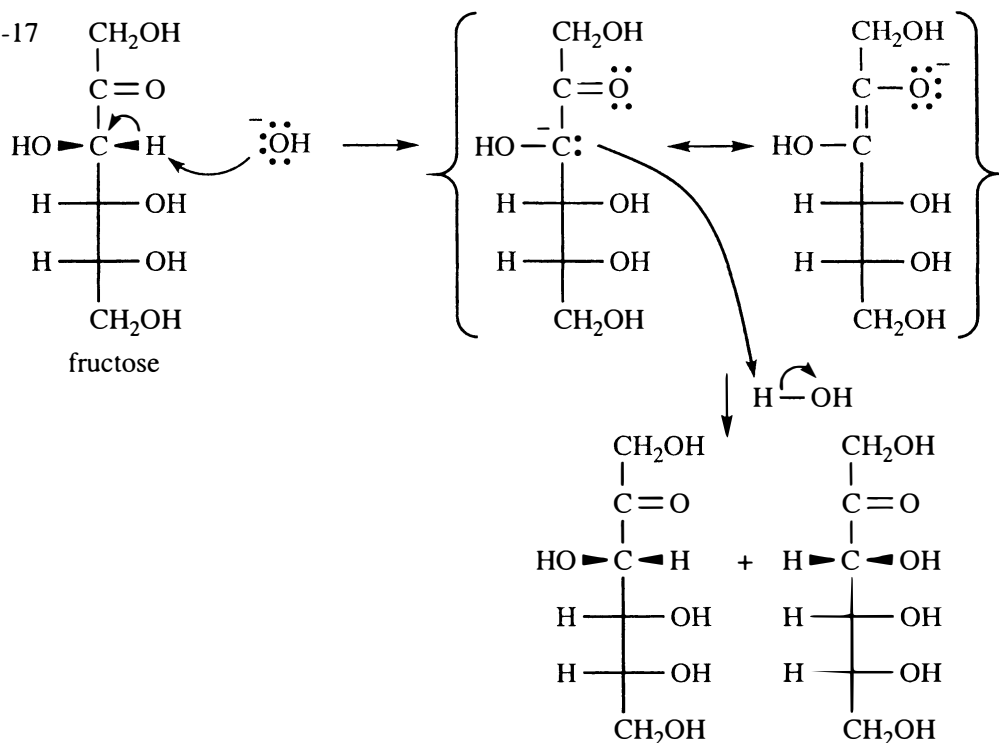
$$a(+150.7^\circ) + (1 - a)(+52.8^\circ) = +80.2^\circ \xrightarrow{\text{solve for "a"}} a = 0.28; \quad b = 0.72$$

The equilibrium mixture contains 28% of the α anomer and 72% of the β anomer.

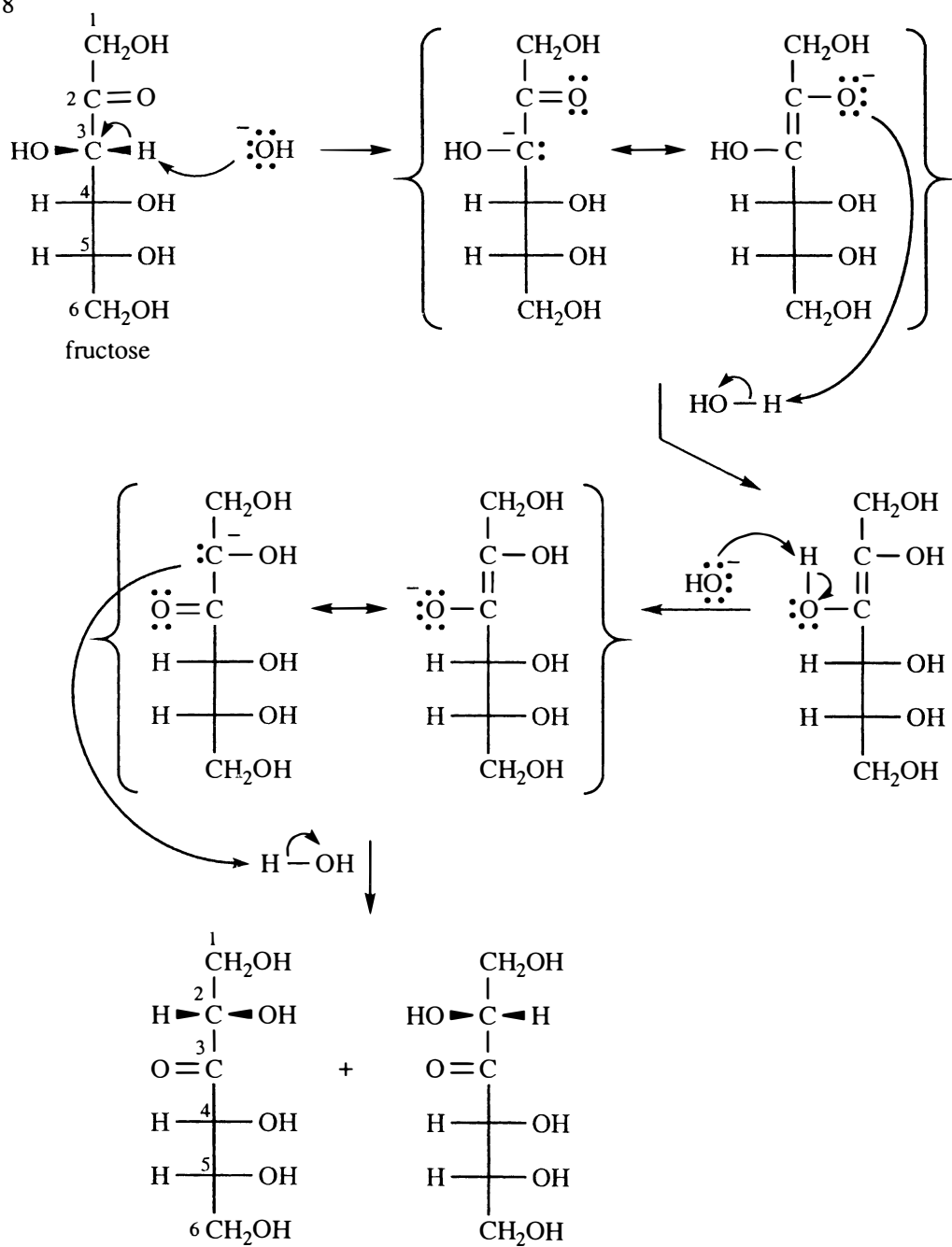
23-16

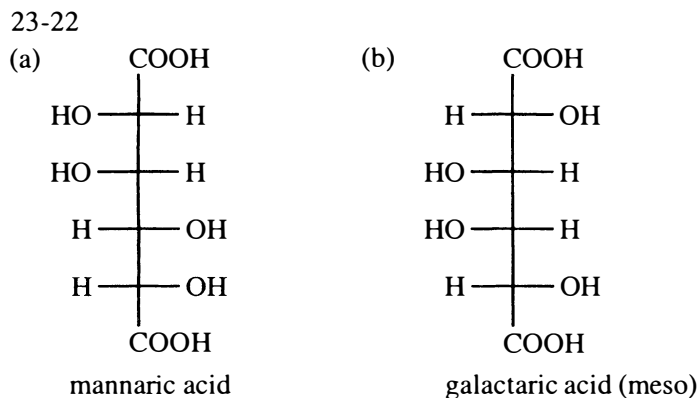
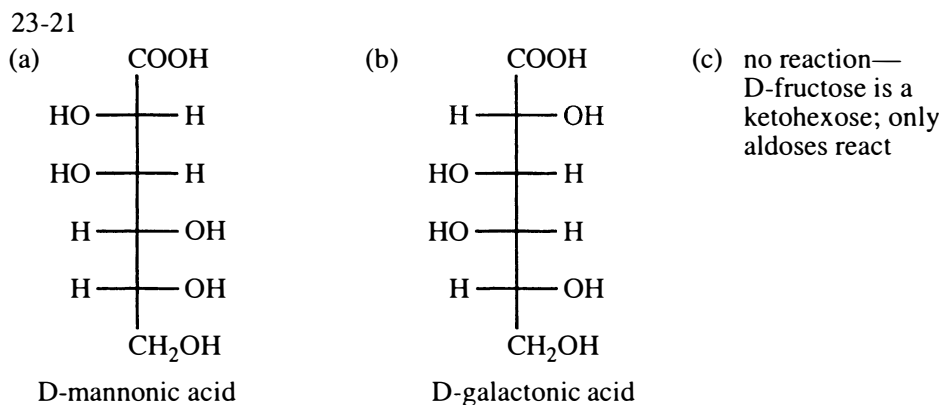
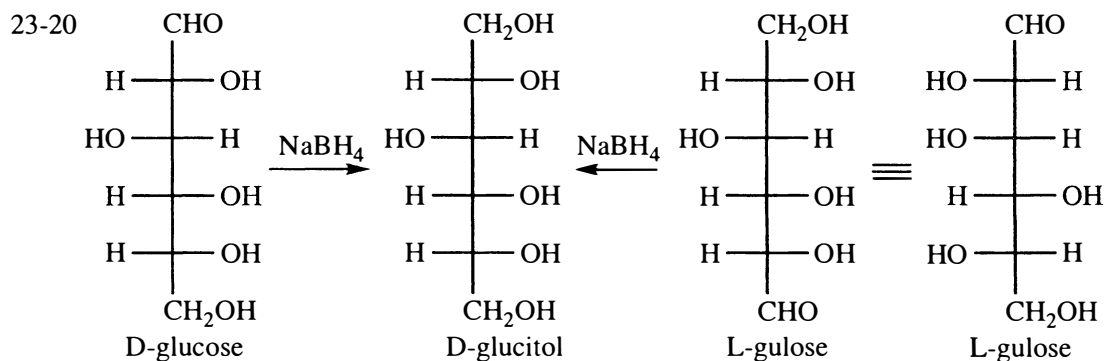
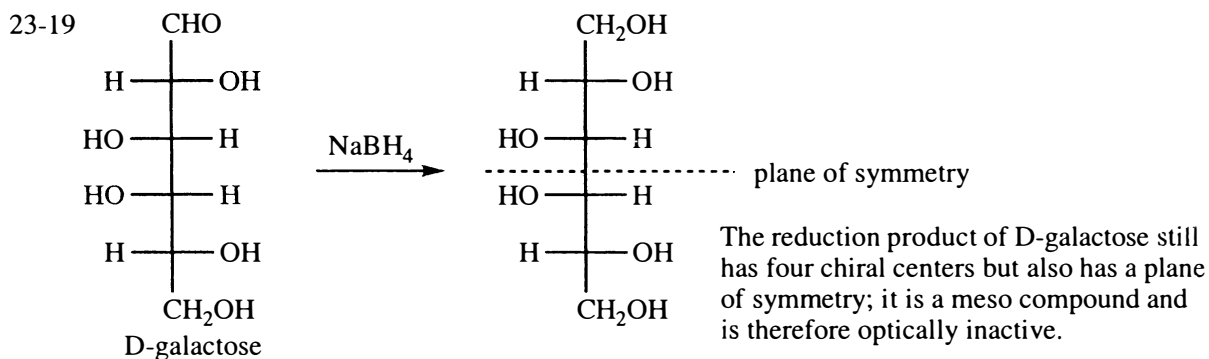


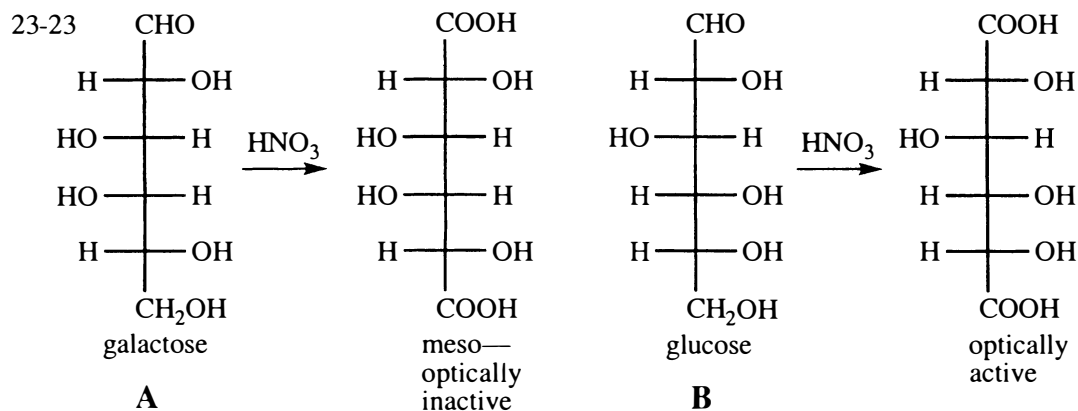
23-17



23-18



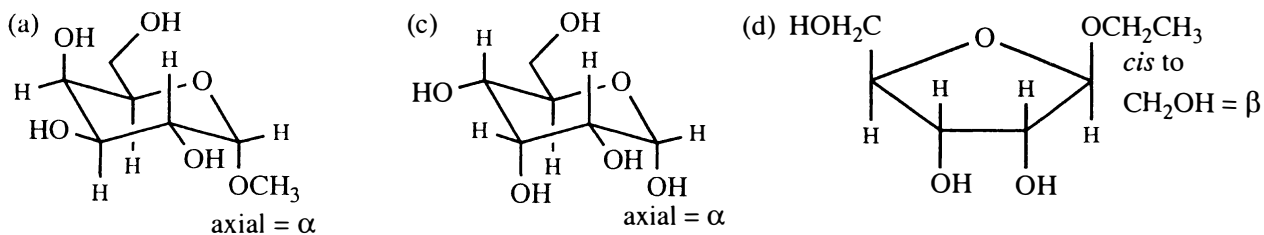




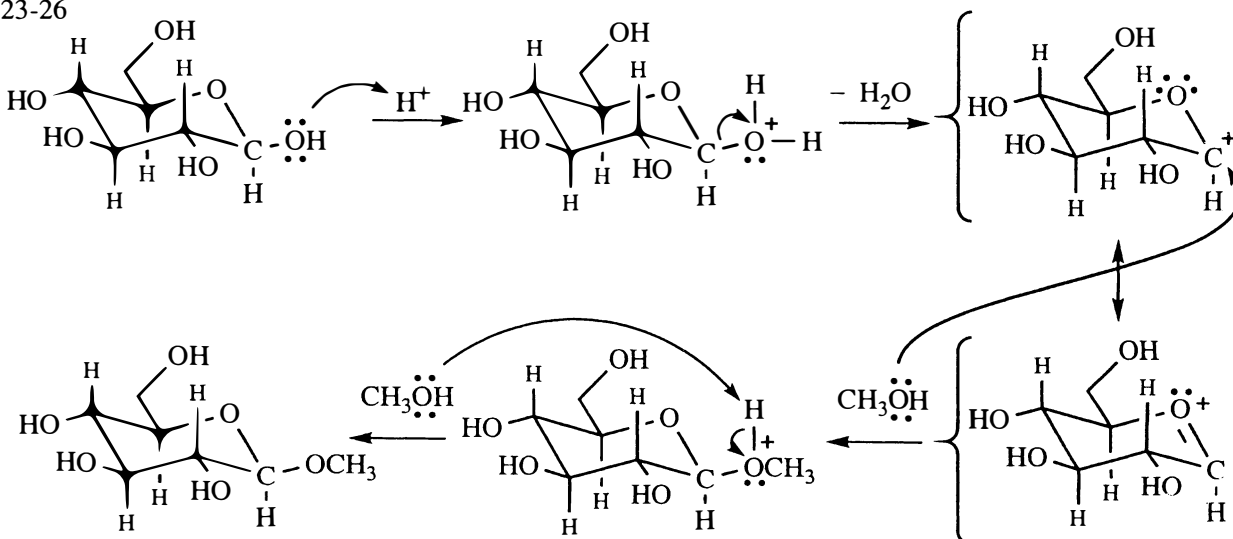
23-24

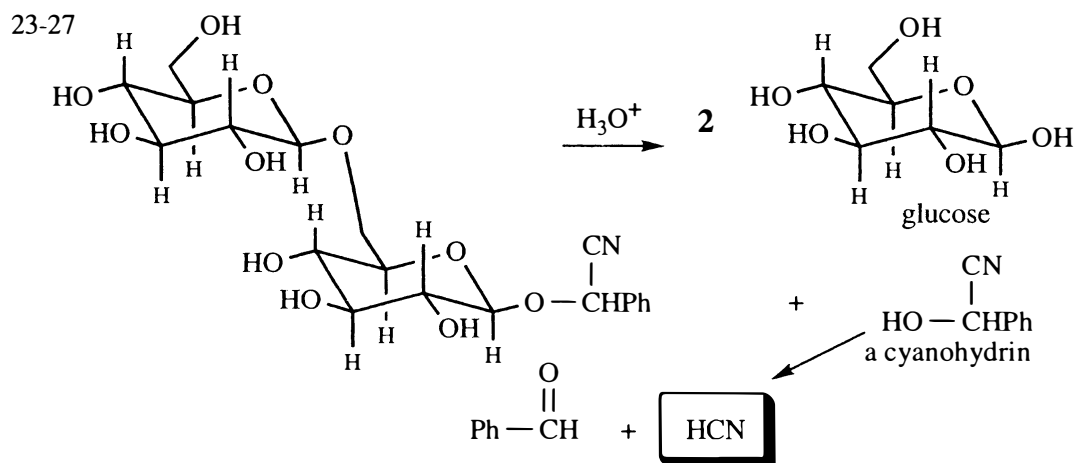
- (a) not reducing: an acetal ending in "oside"
- (b) reducing: a hemiacetal ending in "ose"
- (c) reducing: a hemiacetal ending in "ose"
- (d) not reducing: an acetal ending in "oside"
- (e) reducing: one of the rings has a hemiacetal
- (f) not reducing: all anomeric carbons are in acetal form

23-25



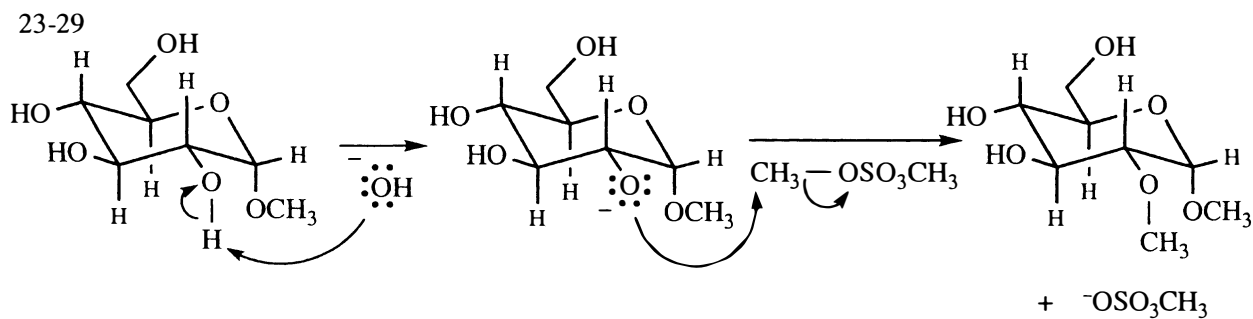
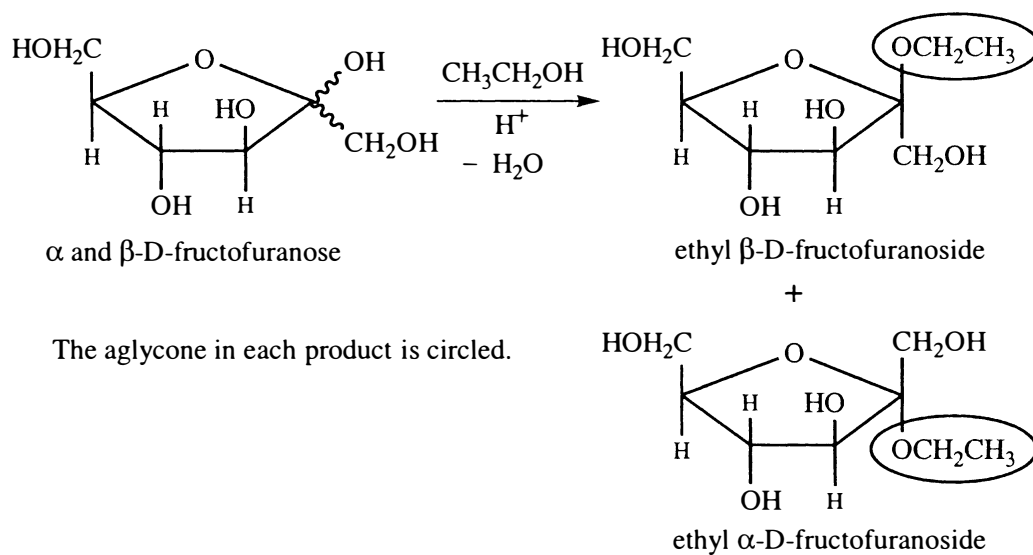
23-26



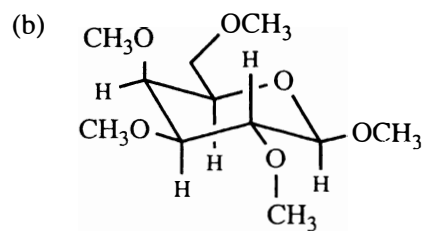
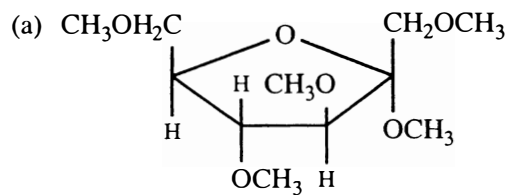


HCN is released from amygdalin. HCN is a potent cytotoxic (cell-killing) agent, particularly toxic to nerve cells.

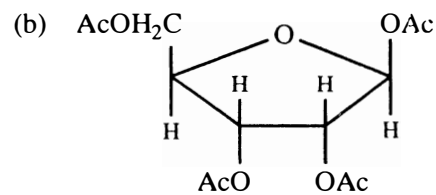
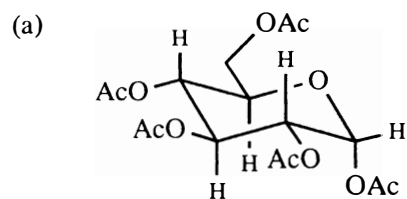
23-28



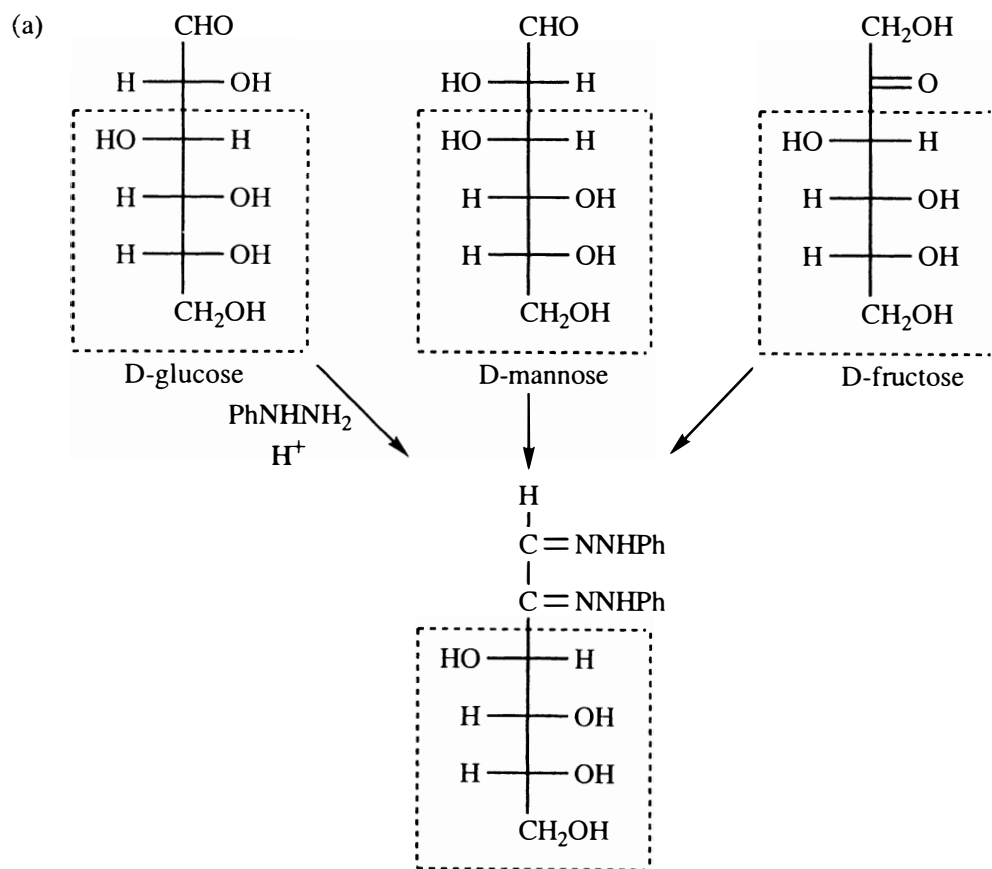
23-30



23-31

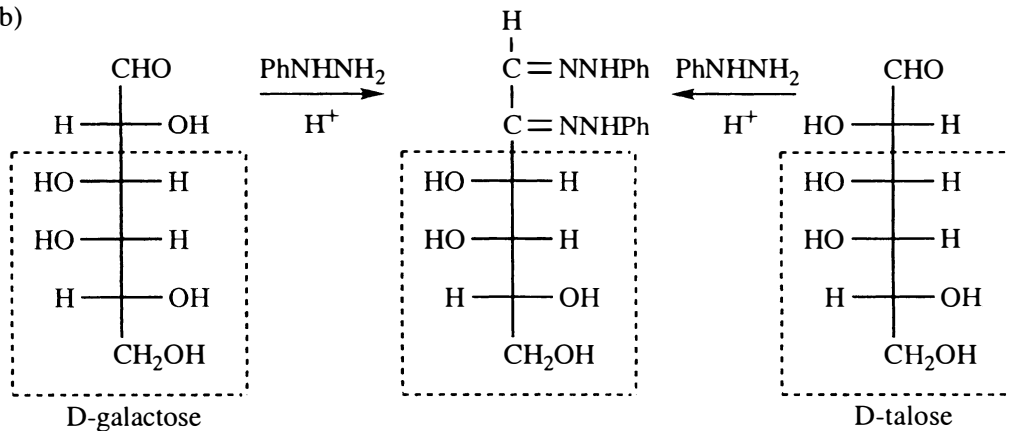


23-32



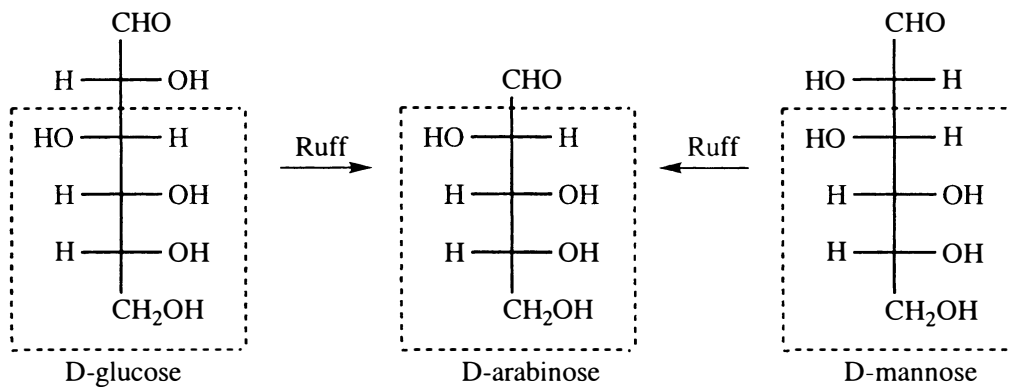
23-32 continued

(b)

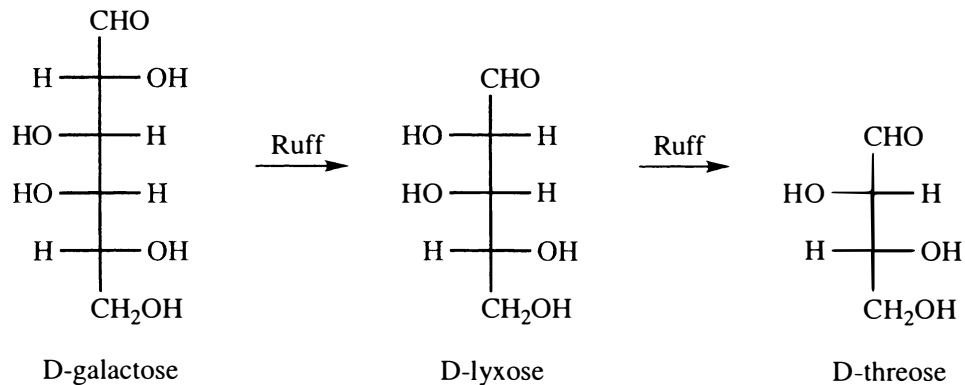


D-Talose must be the C-2 epimer of D-galactose.

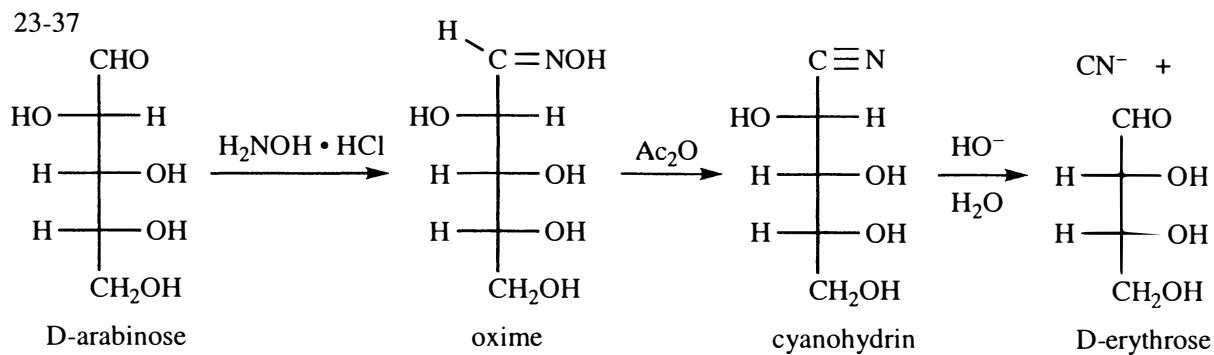
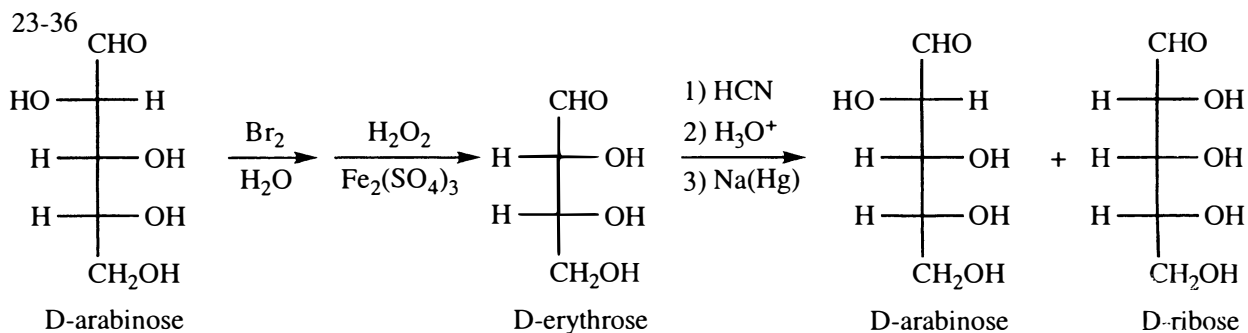
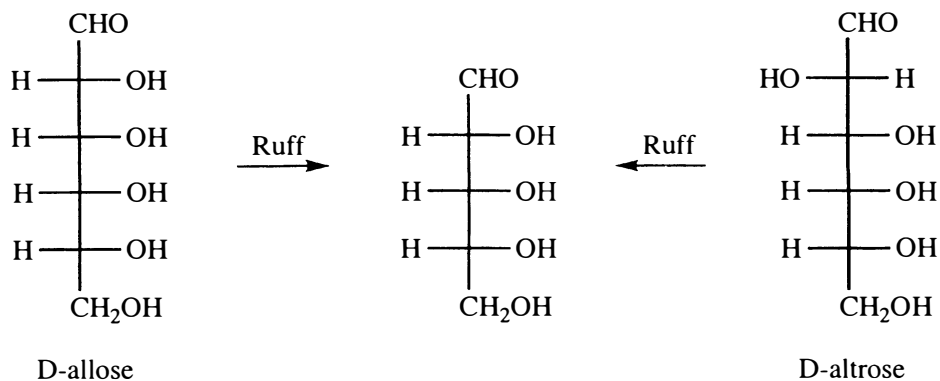
23-33 Reagents for the Ruff degradation are: 1. Br₂, H₂O; 2. H₂O₂, Fe₂(SO₄)₃.



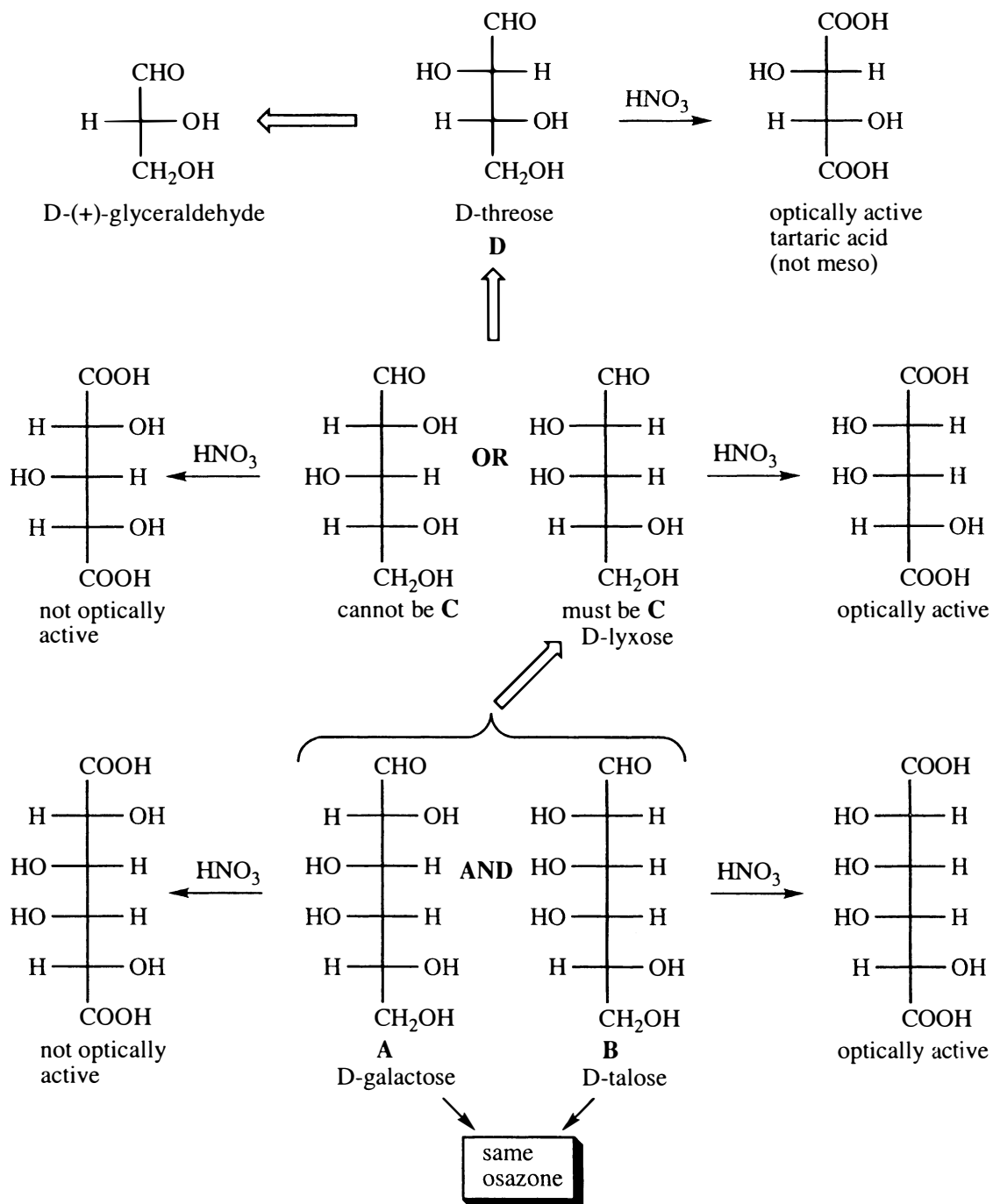
23-34 Reagents for the Ruff degradation are: 1. Br₂, H₂O; 2. H₂O₂, Fe₂(SO₄)₃.



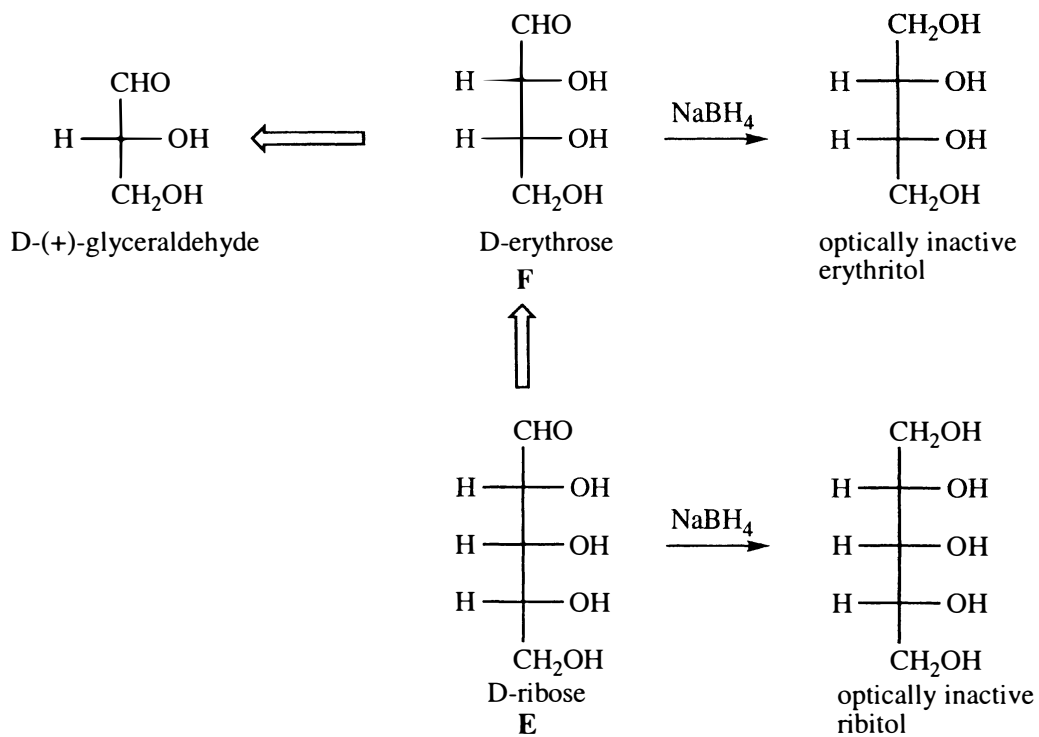
23-35 Reagents for the Ruff degradation are: 1. $\text{Br}_2, \text{H}_2\text{O}$; 2. $\text{H}_2\text{O}_2, \text{Fe}_2(\text{SO}_4)_3$.



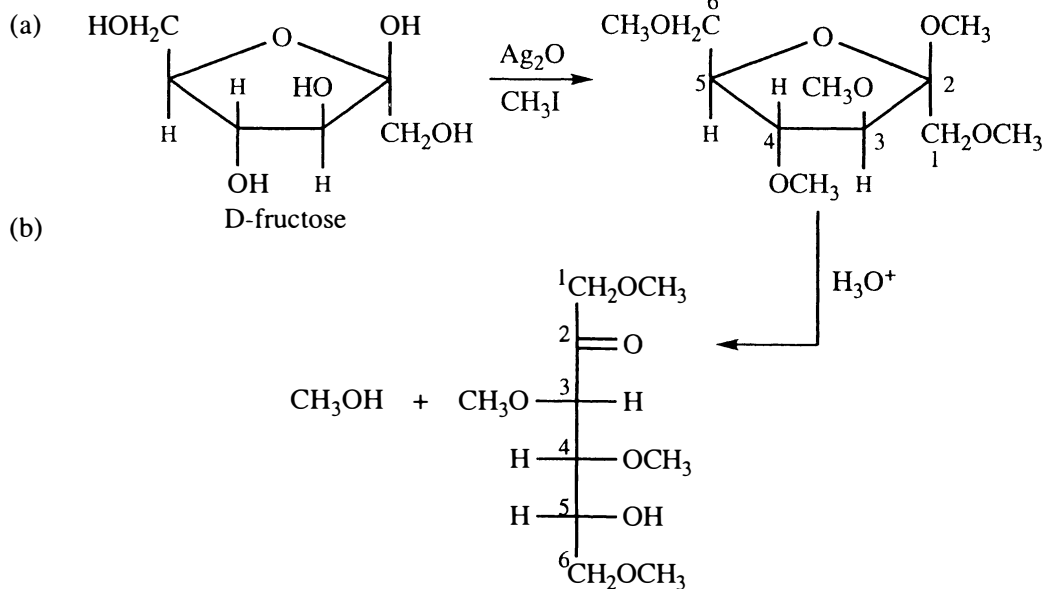
23-38 Solve this problem by working backward from (+)-glyceraldehyde.



23-39 Solve this problem by working backward from (+)-glyceraldehyde.

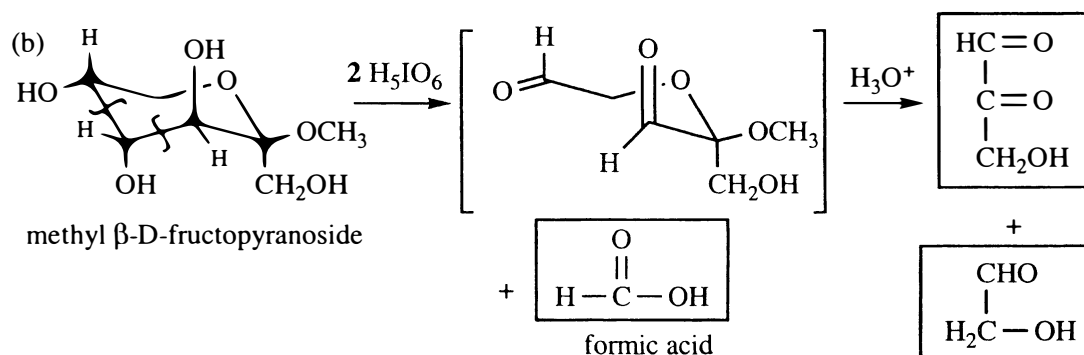
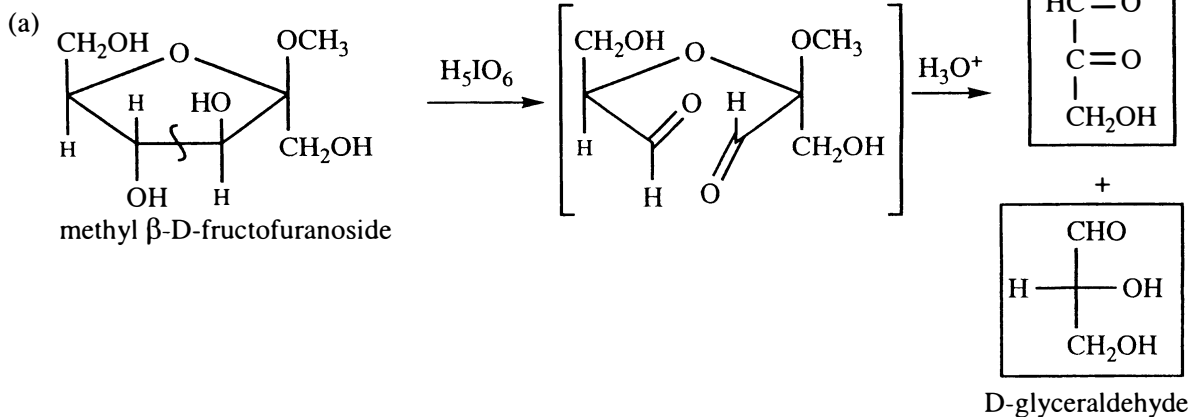


23-40



(c) Determining that the open chain form of fructose is a ketone at C-2 with a free OH at C-5 shows that fructose exists as a furanose hemiacetal.

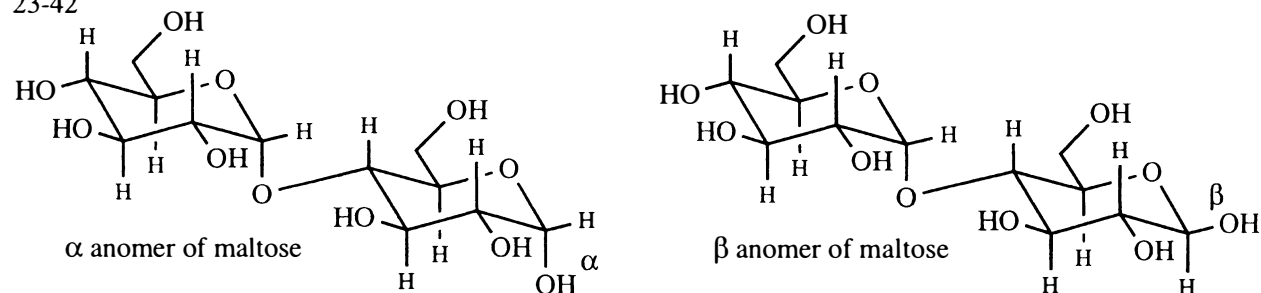
23-41

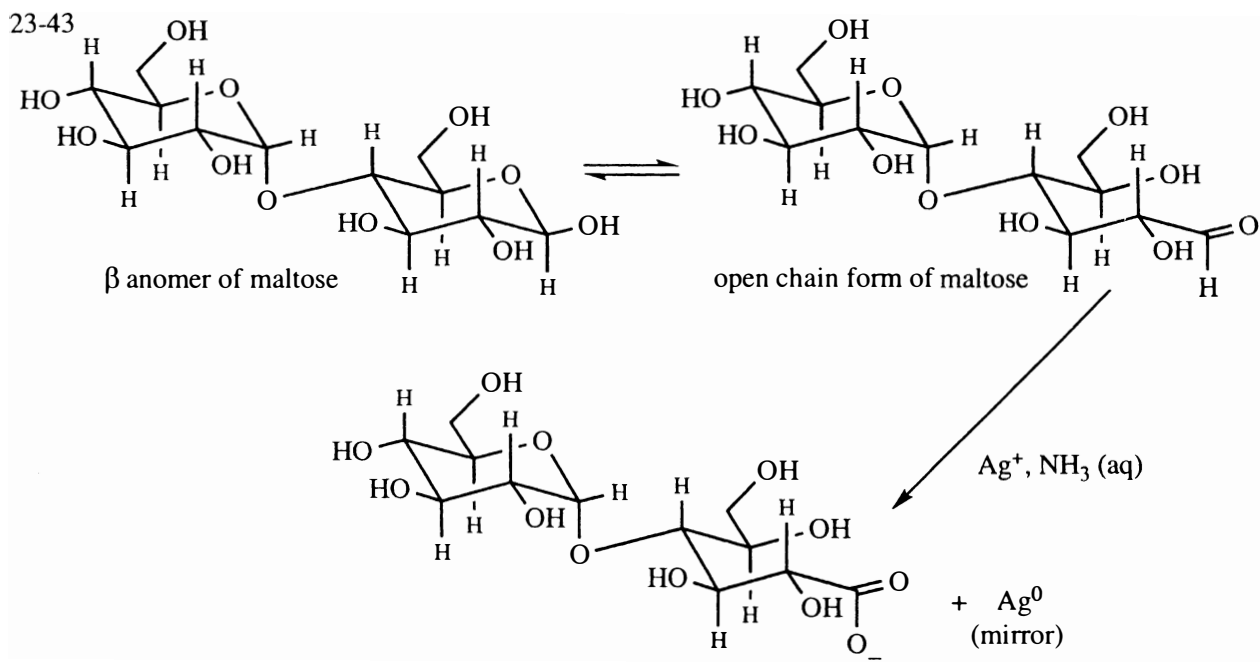


Production of one equivalent of formic acid, and two fragments containing two and three carbons respectively, proves that the glycoside was in a six-membered ring.

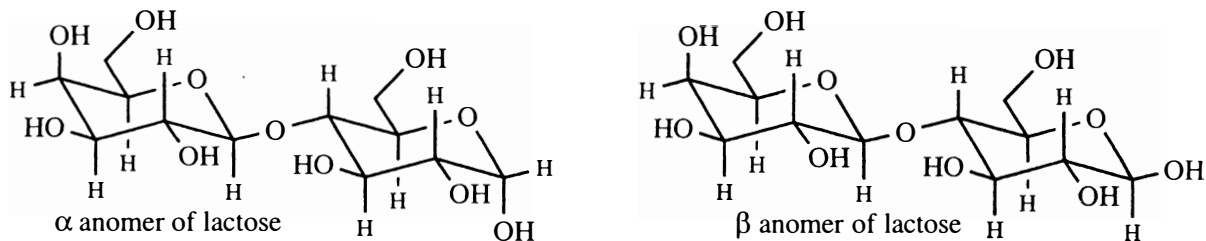
(c) In periodic acid oxidation of an aldohexose glycoside, glyceraldehyde is generated from carbons 4, 5, and 6. If configuration at the middle carbon is D, that means that carbon-5 of the aldohexose must have had the D configuration. On the other hand, if the isolated glyceraldehyde had the L configuration, then the original aldohexose must have been an L sugar.

23-42



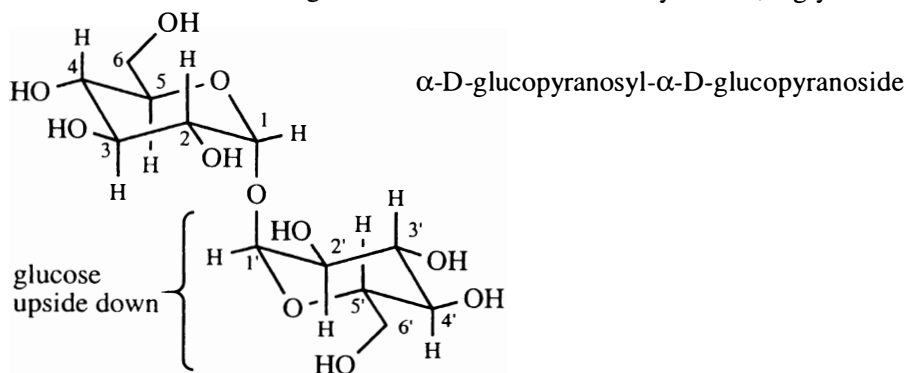


23-44 Lactose is a hemiacetal. Therefore, it can mutarotate and is a reducing sugar.

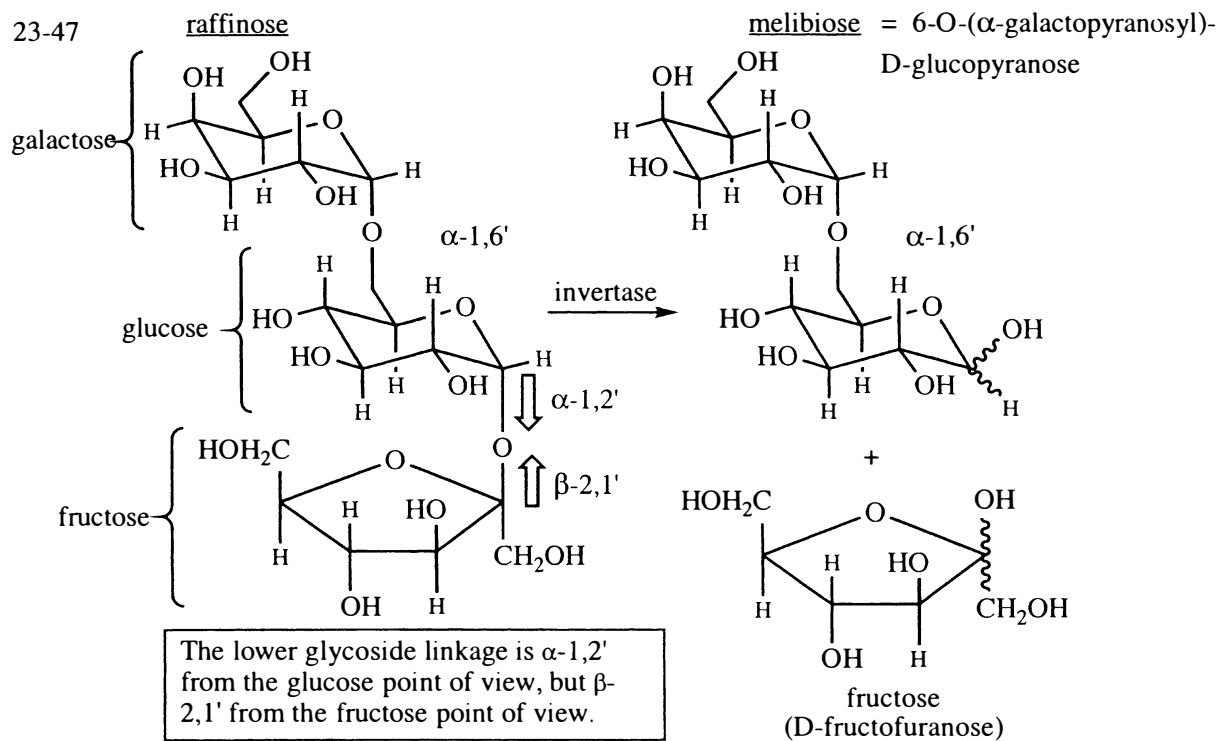


23-45 Gentiobiose is a hemiacetal; in water, the hemiacetal is in equilibrium with the open-chain form and can react as an aldehyde. Gentiobiose can mutarotate and is a reducing sugar.

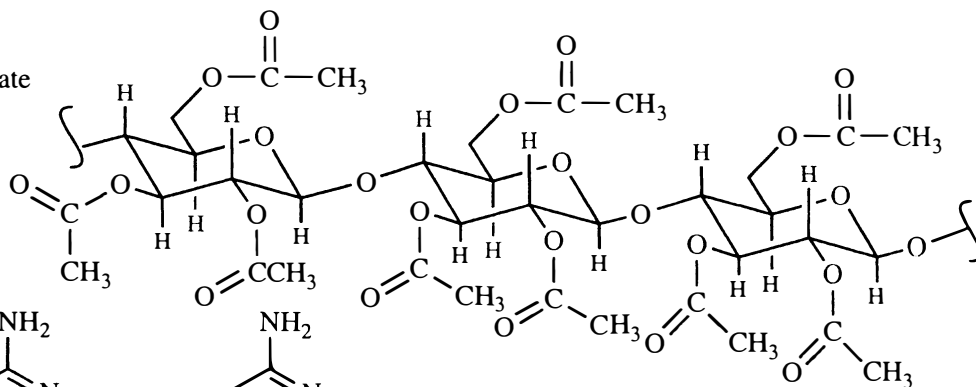
23-46 Trehalose must be two glucose molecules connected by an α -1,1'-glycoside.



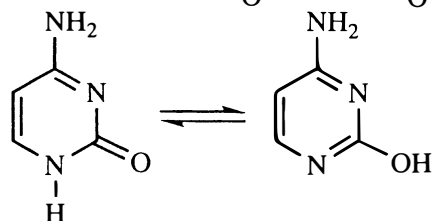
23-47



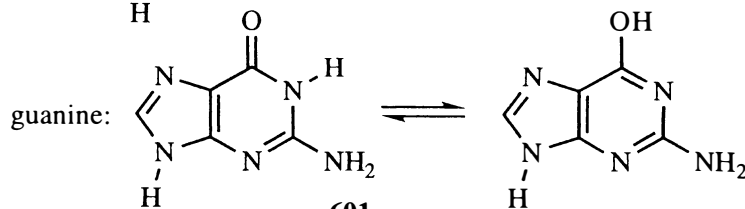
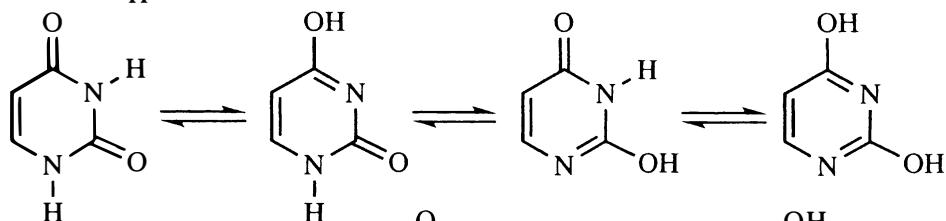
23-48 cellulose acetate



23-49 cytosine:

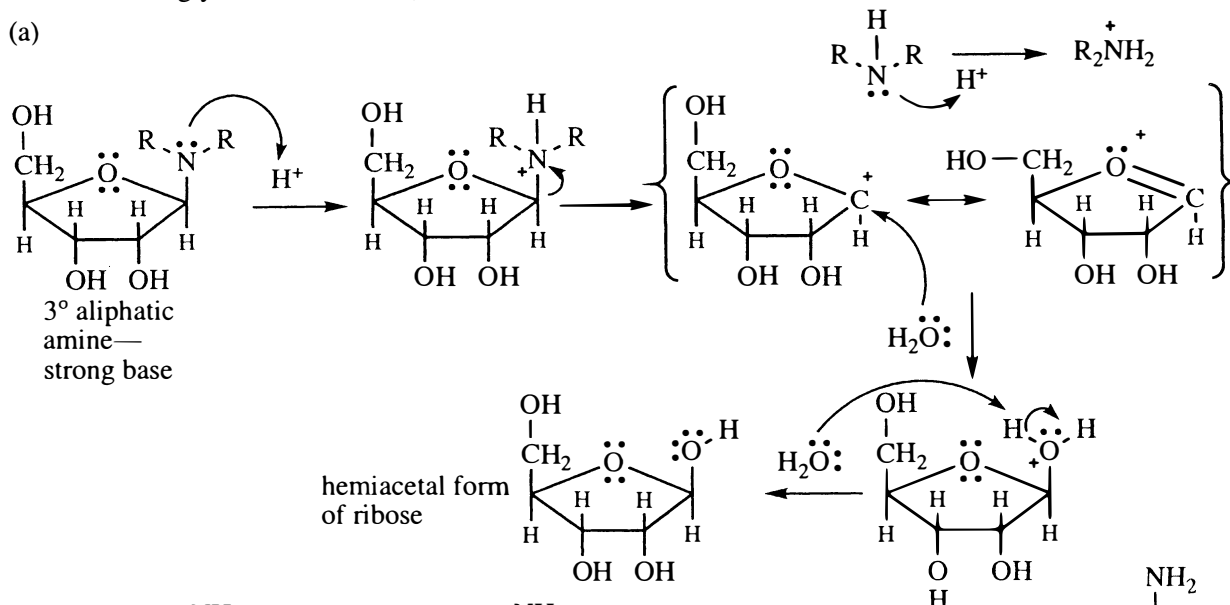


uracil:

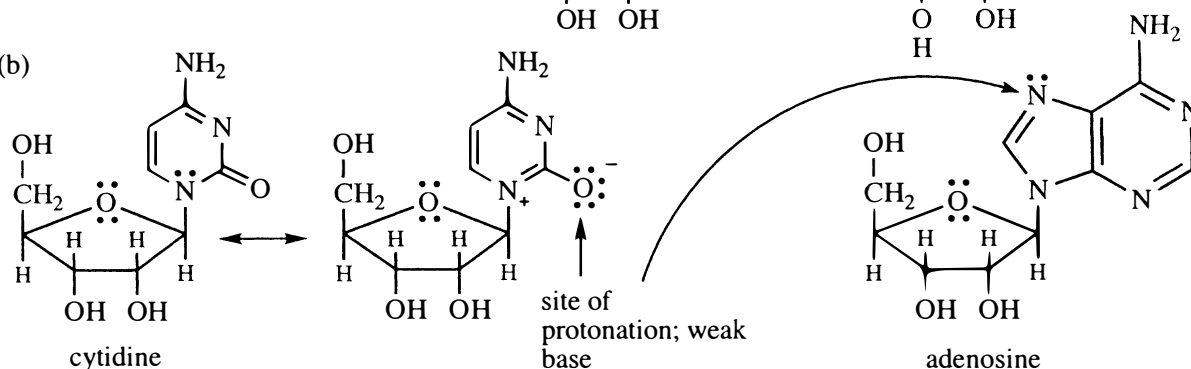


23-50 Aminoglycosides, including nucleosides, are similar to acetals: stable to base, cleaved by acid.

(a)



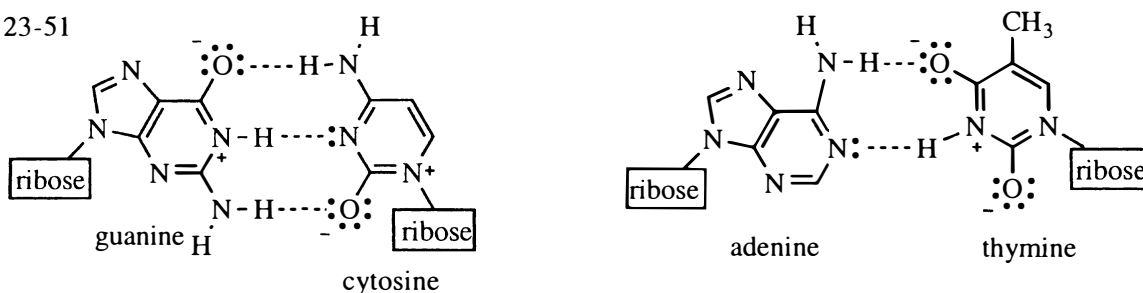
(b)



Nucleosides are less rapidly hydrolyzed in aqueous acid because the site of protonation (the N in adenosine, and in cytidine, the oxygen shown with the negative charge in the second resonance form) is much less basic than the aliphatic amine in an aminoglycoside. Nucleosides require stronger acid, or longer time and higher temperature, to be hydrolyzed.

This is important in living systems as it would cause genetic damage or even death of an organism if its DNA or RNA were too easily decomposed. Organisms go to great length and expend considerable energy to maintain the structural integrity of their DNA.

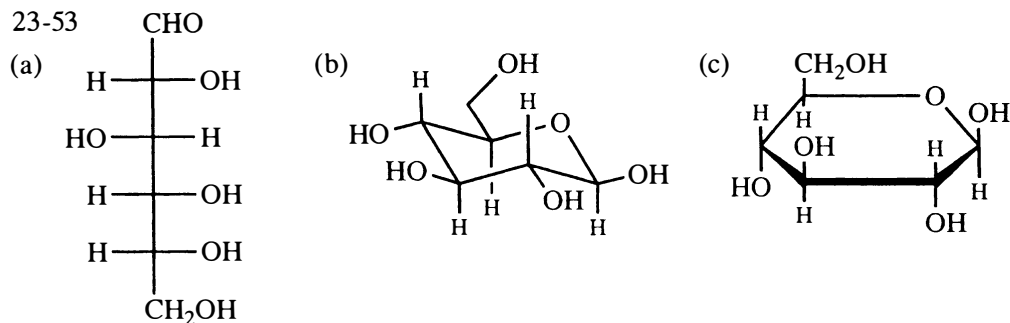
23-51



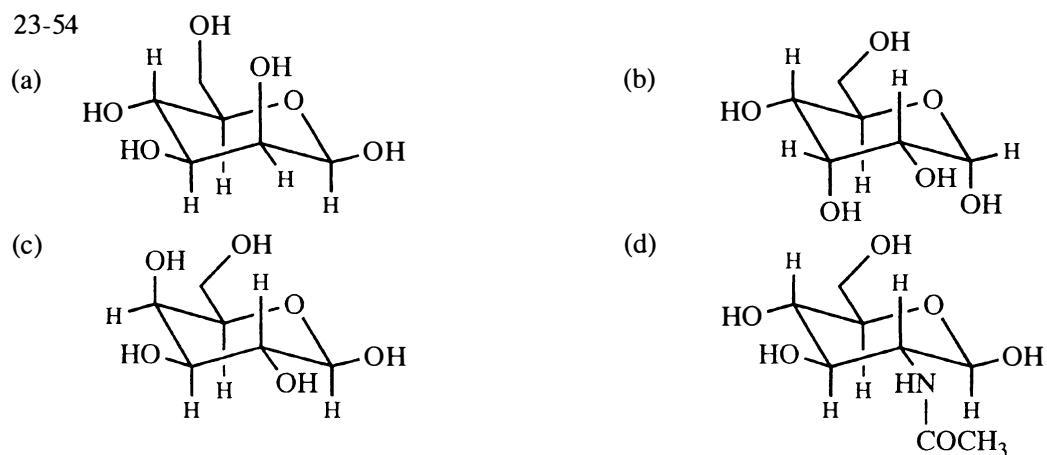
The polar resonance forms show how the hydrogen bonds are particularly strong. Each oxygen has significant negative charge, and in each pair, one H—N is polarized more strongly because the N has positive charge.

23-52 Please refer to solution 1-20, page 12 of this Solutions Manual.

23-53



23-54

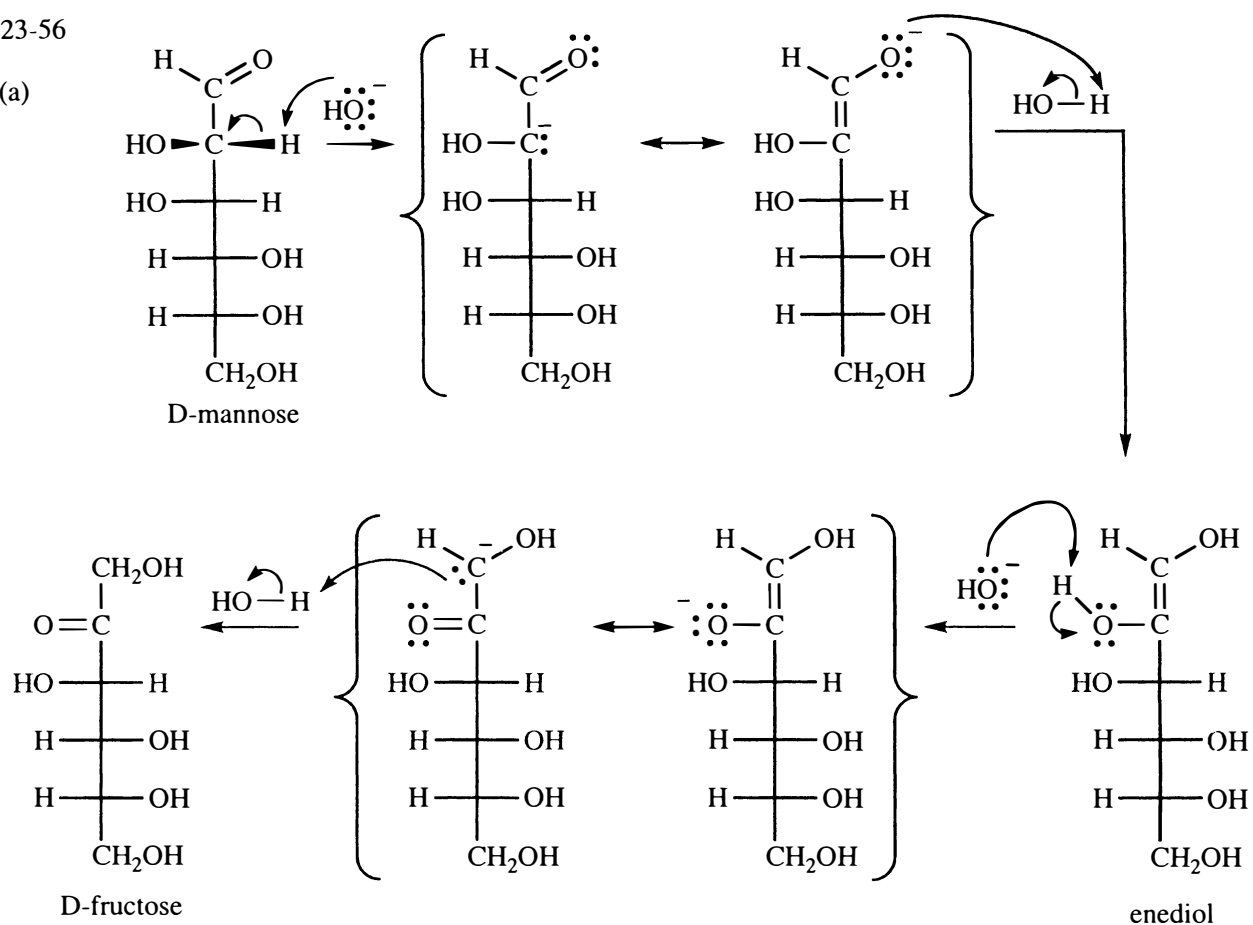


23-55

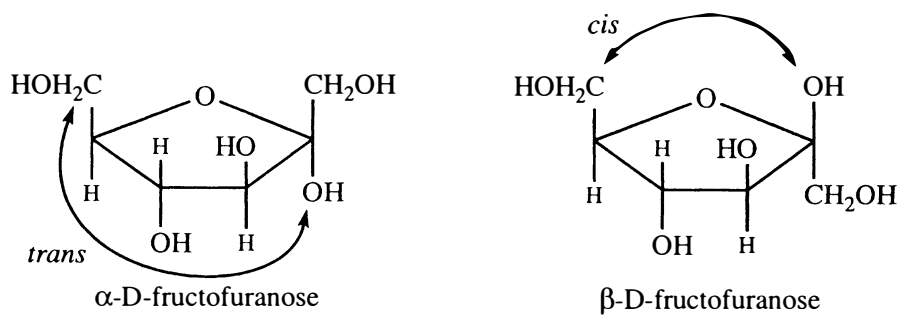
- (a) D-aldohexose (D configuration, aldehyde, 6 carbons)
- (b) D-aldopentose (D configuration, aldehyde, 5 carbons)
- (c) L-ketohexose (L configuration, ketone, 6 carbons)
- (d) L-aldohexose (L configuration, aldehyde, 6 carbons)
- (e) D-ketopentose (D configuration, ketone, 5 carbons)
- (f) L-aldotetrose (L configuration, aldehyde, 4 carbons)
- (g) 2-acetamido D-aldohexose (D configuration, aldehyde, 6 carbons in chain, with acetamido group at C-2)

23-56

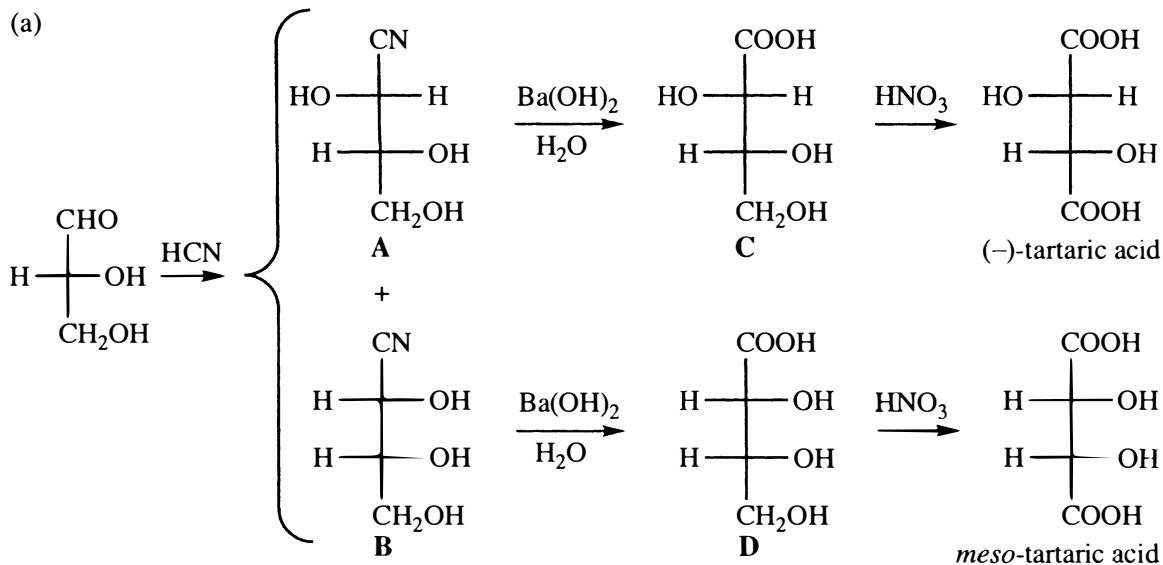
(a)



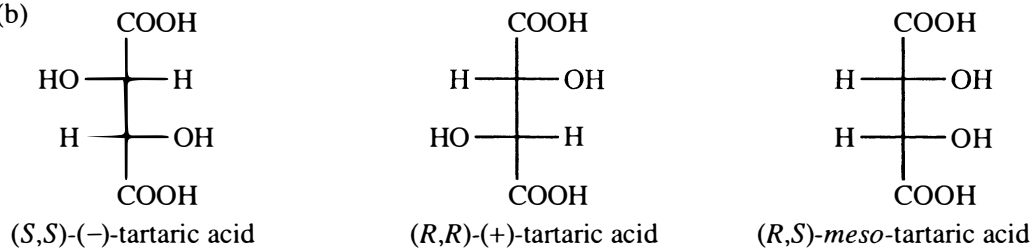
(b) The α isomer has the anomeric OH *trans* to the CH_2OH off of C-5. The β -anomer has these groups *cis*.



23-57



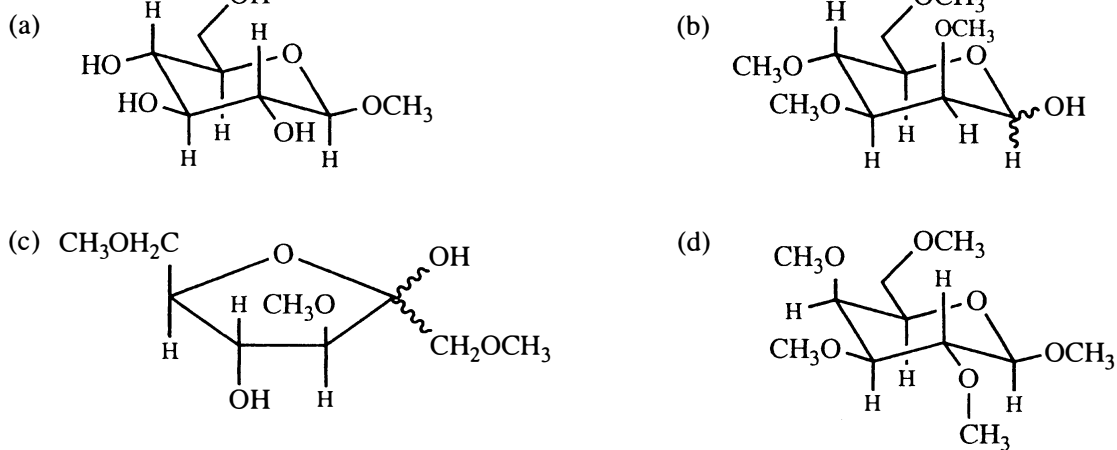
(b)



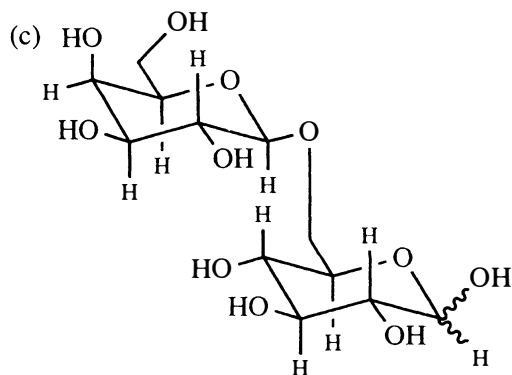
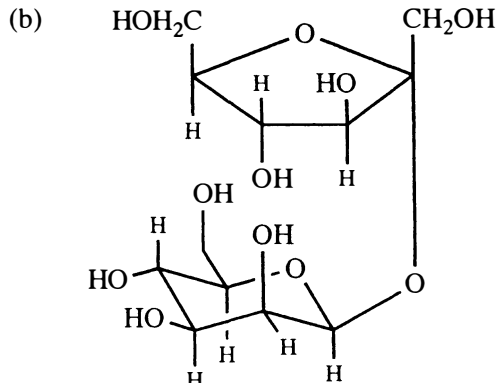
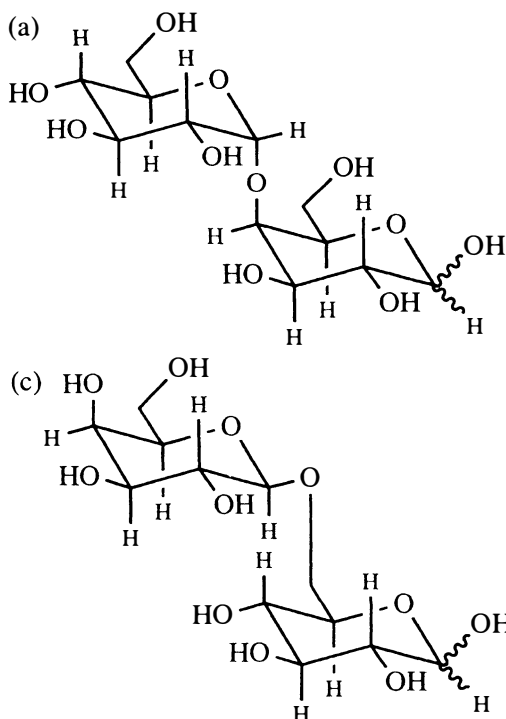
23-58

(a) D-(-)-ribose (b) D-(+)-altrose (c) L-(+)-erythrose (d) L-(-)-galactose (e) L-(+)-idose

23-59



23-60



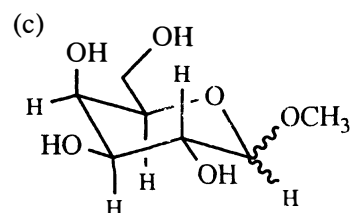
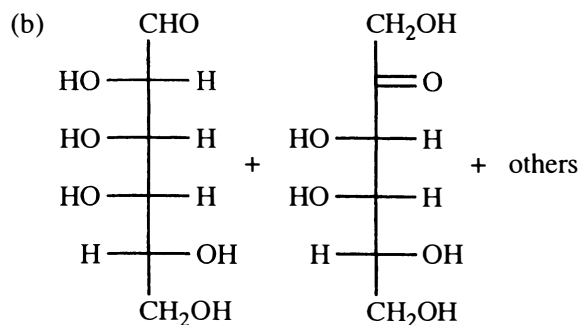
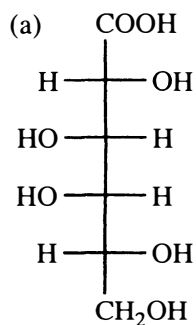
23-61

- (a) methyl β -D-fructofuranoside
 (b) 3,6-di-O-methyl- β -D-mannopyranose
 (c) 4-O-(α -D-fructofuranosyl)- β -D-galactopyranose
 (d) β -D-N-acetylgalactopyranosamine, or 2-acetamido-2-deoxy- β -D-galactopyranose

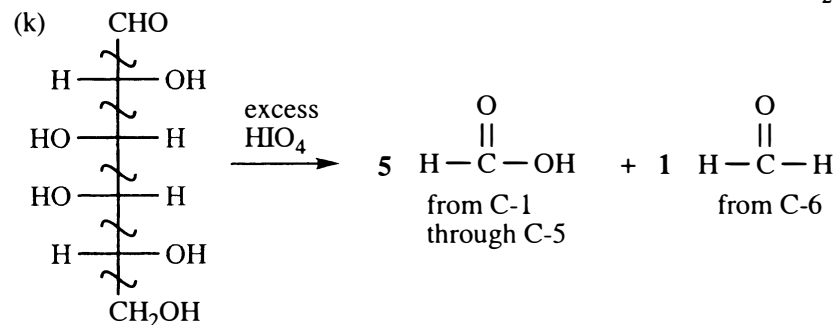
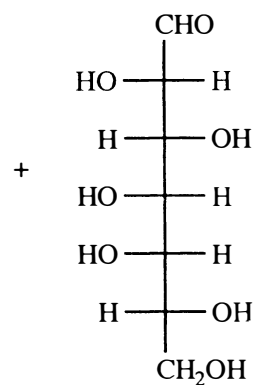
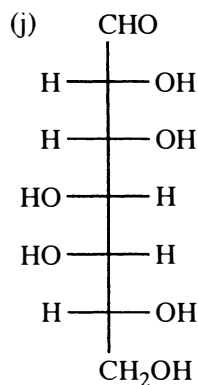
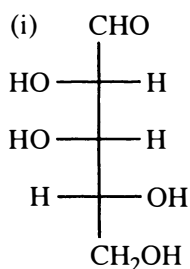
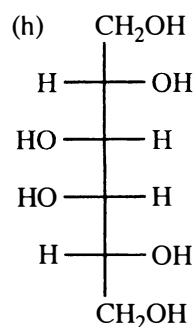
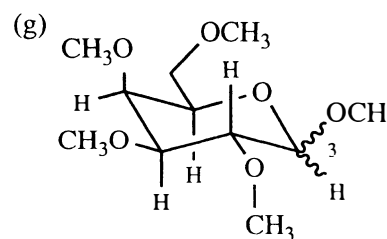
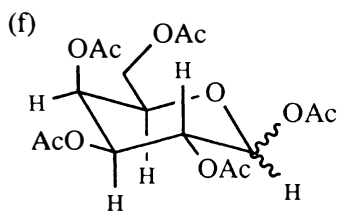
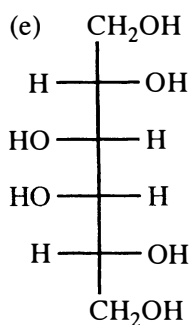
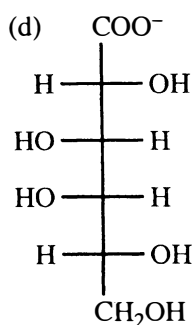
23-62 These are reducing sugars and would undergo mutarotation:

- in problem 23-59: (b) and (c);
 —in problem 23-60: (a) and (c);
 —in problem 23-61: (b), (c), and (d)

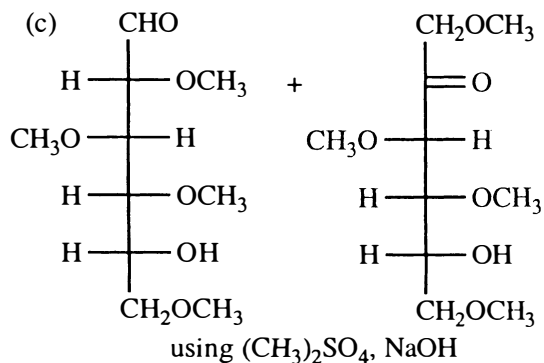
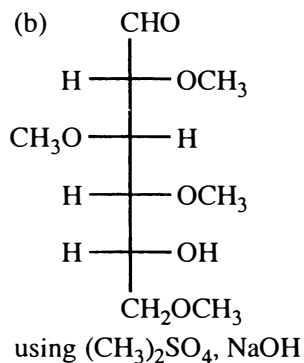
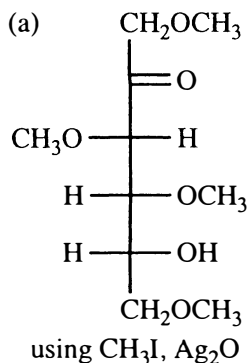
23-63



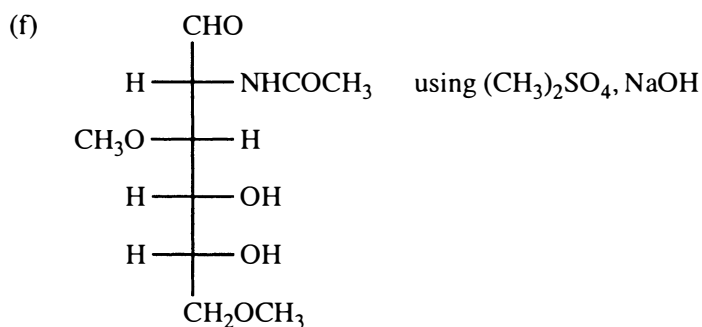
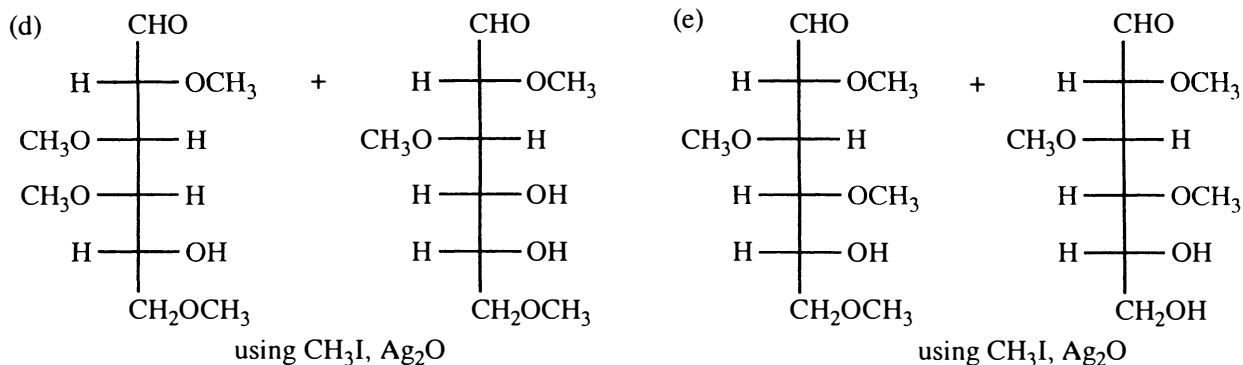
23-63 continued



23-64 Use the milder reagent, $\text{CH}_3\text{I}/\text{Ag}_2\text{O}$, when the sugar is in the hemiacetal form; the mild conditions prevent isomerization. When the carbohydrate is present as an acetal (a glycoside), use the more basic reagent, $\text{NaOH}/(\text{CH}_3)_2\text{SO}_4$; an acetal is stable to basic conditions.

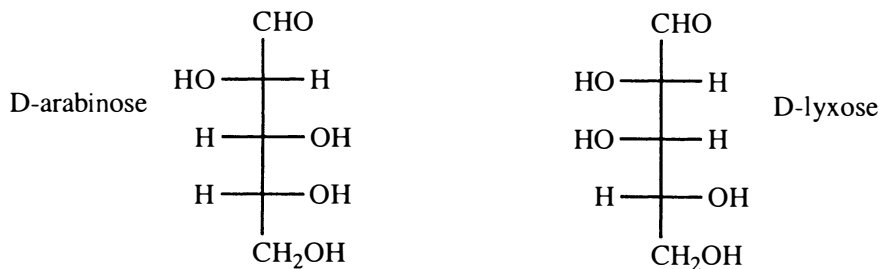


23-64 continued

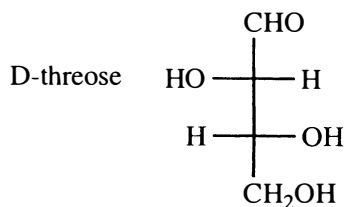


23-65

(a) These D-aldopentoses will give optically active aldaric acids.

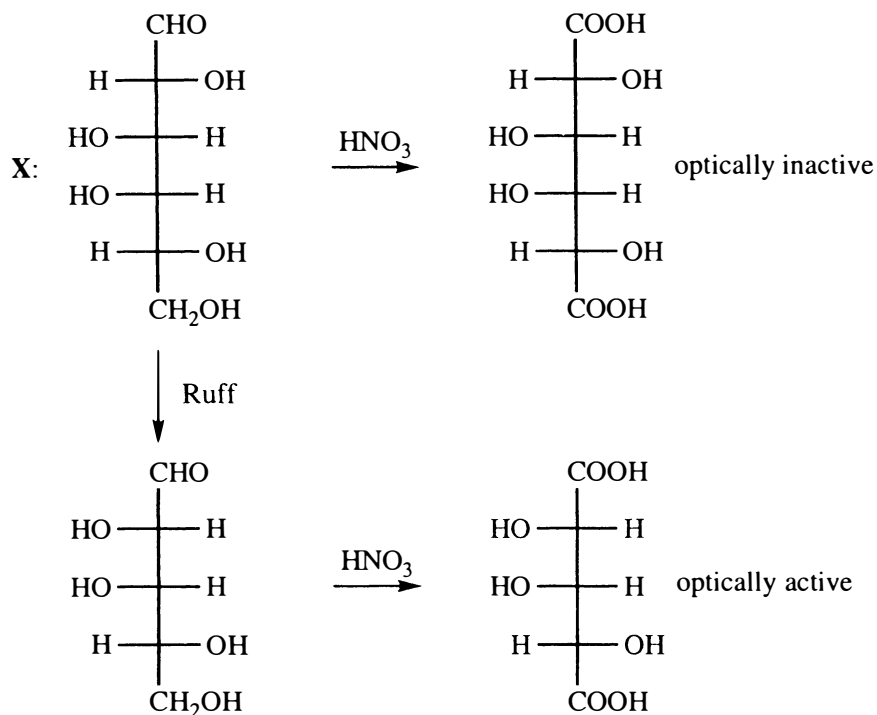


(b) Only D-threose (of the aldotetroses) will give an optically active aldaric acid.



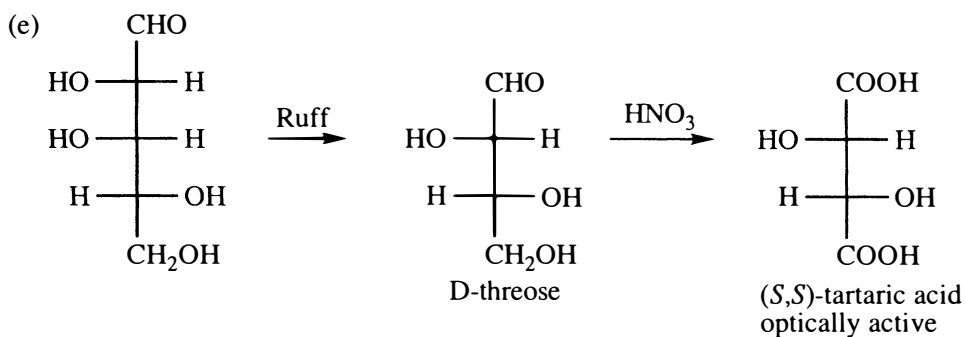
23-65 continued

(c) **X** is D-galactose.



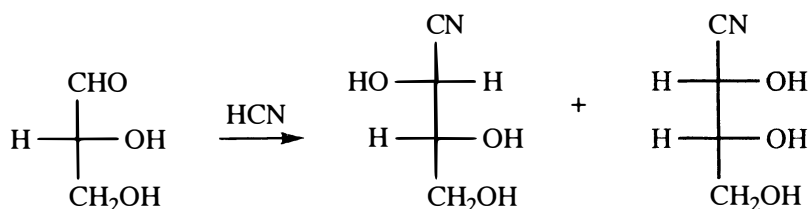
The other aldohexose that gives an optically inactive aldaric acid is D-allose, with all OH groups on the right side of the Fischer projection. Ruff degradation followed by nitric acid gives an optically *inactive* aldaric acid, however, so **X** cannot be D-allose.

(d) The optically active, five-carbon aldaric acid comes from the optically active pentose, not from the optically inactive, six-carbon aldaric acid. The principle is not violated.



23-66

(a)

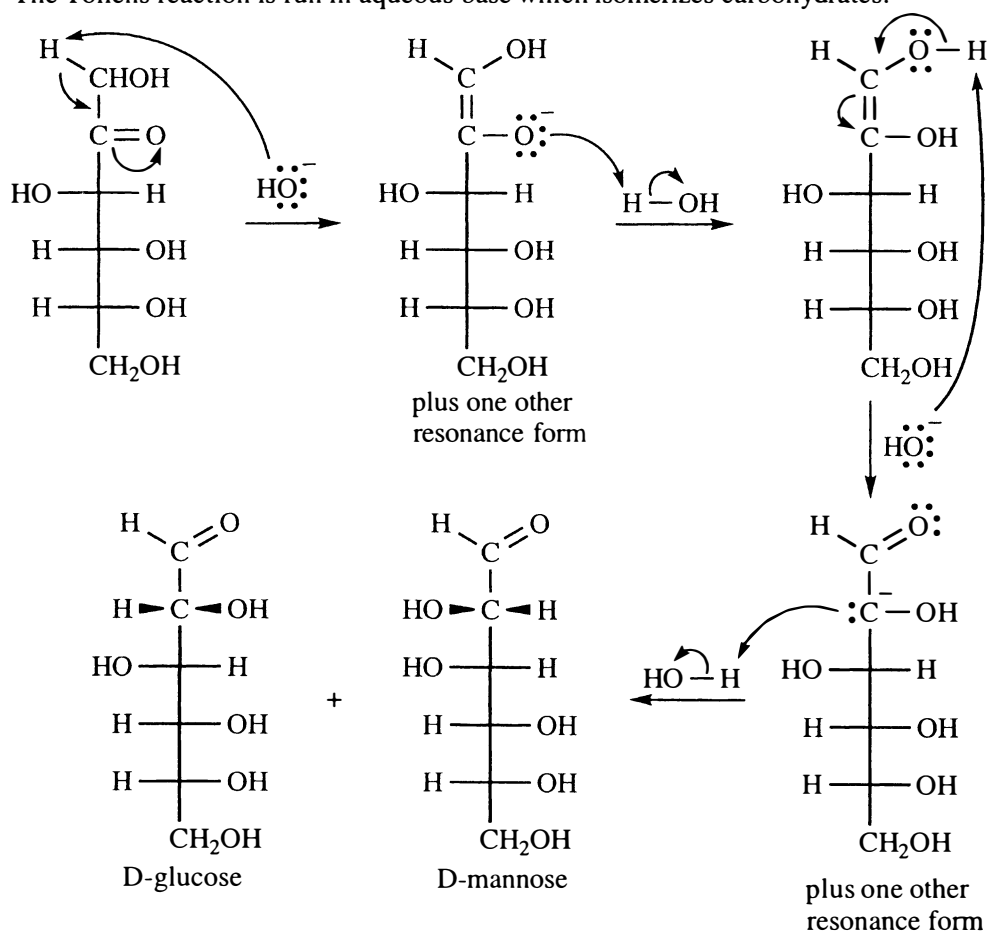


(b) The products are diastereomers with different physical properties. They could be separated by crystallization, distillation, or chromatography.

(c) Both products are optically active. Each has two chiral centers and no plane of symmetry.

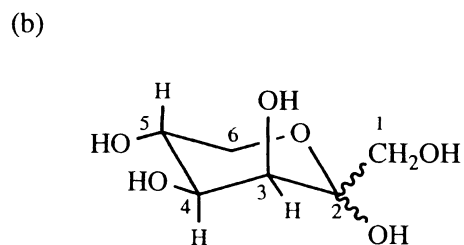
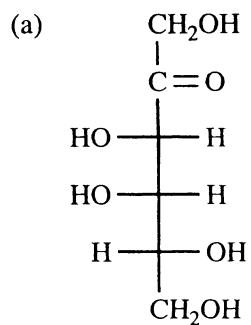
23-67

(a) The Tollens reaction is run in aqueous base which isomerizes carbohydrates.

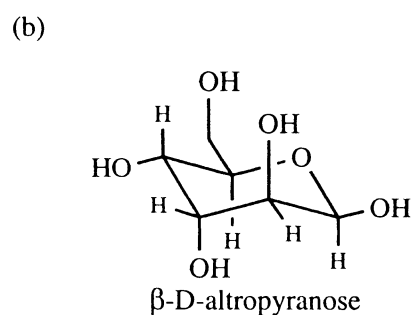
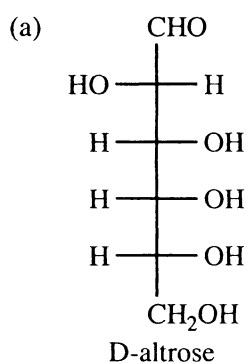


(b) Bromine water is acidic, not basic like the Tollens reagent. Carbohydrates isomerize quickly in base, but only very slowly in acid, so bromine water can oxidize without isomerization.

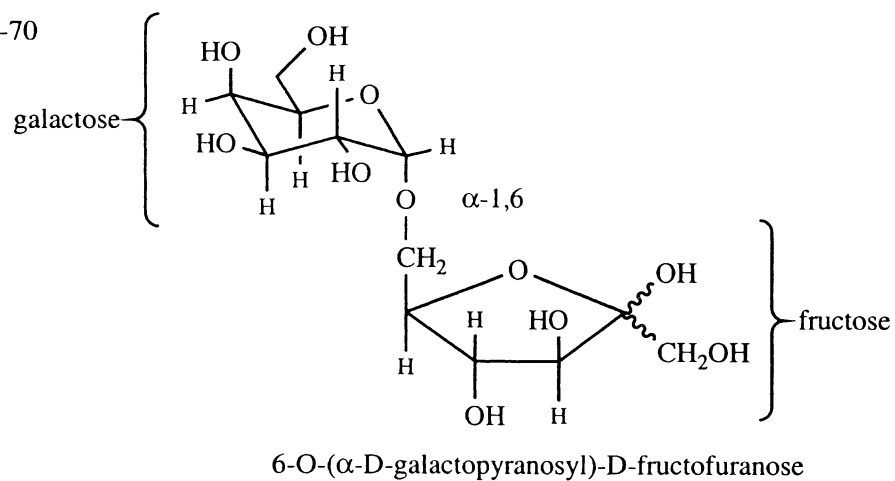
23-68 Tagatose is a monosaccharide, a ketohexose, that is found in the pyranose form.

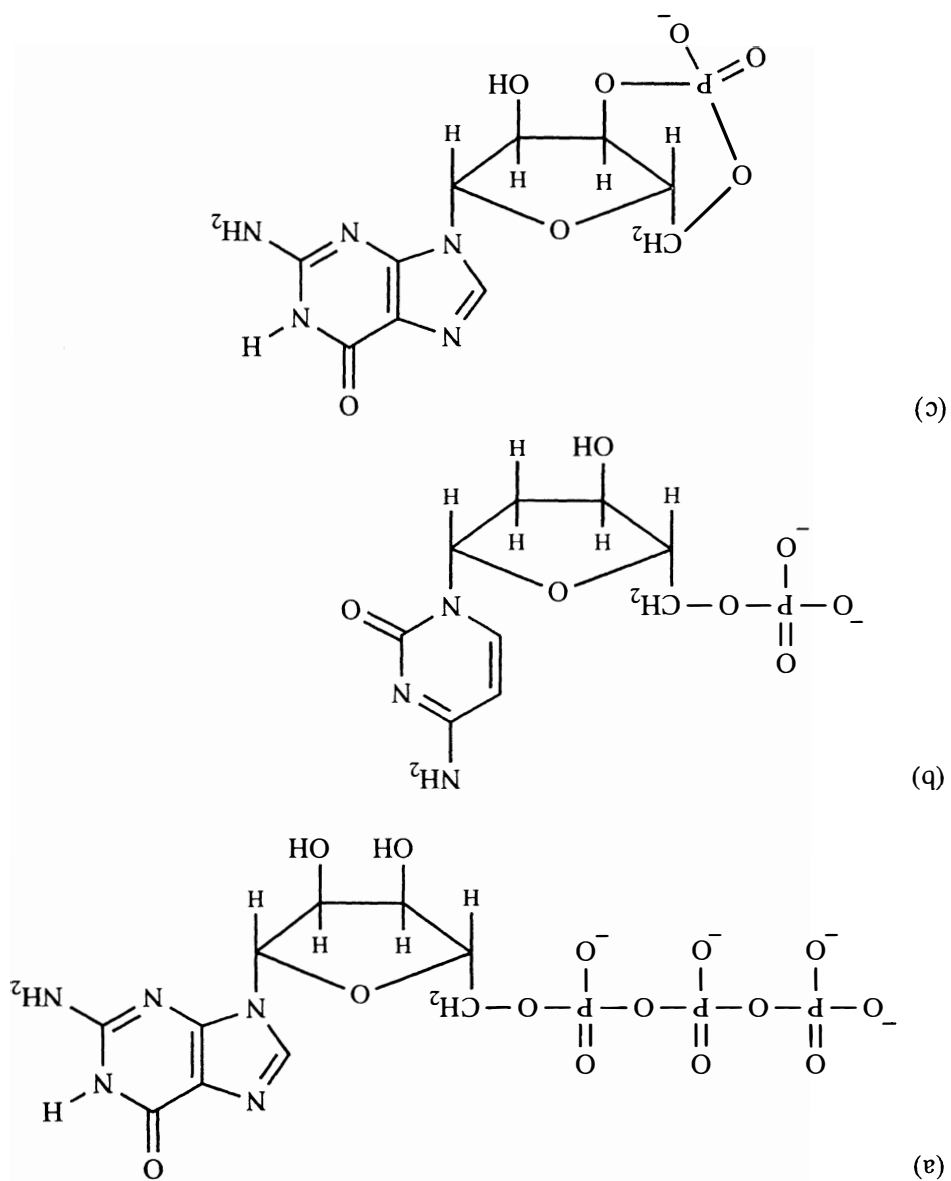


23-69

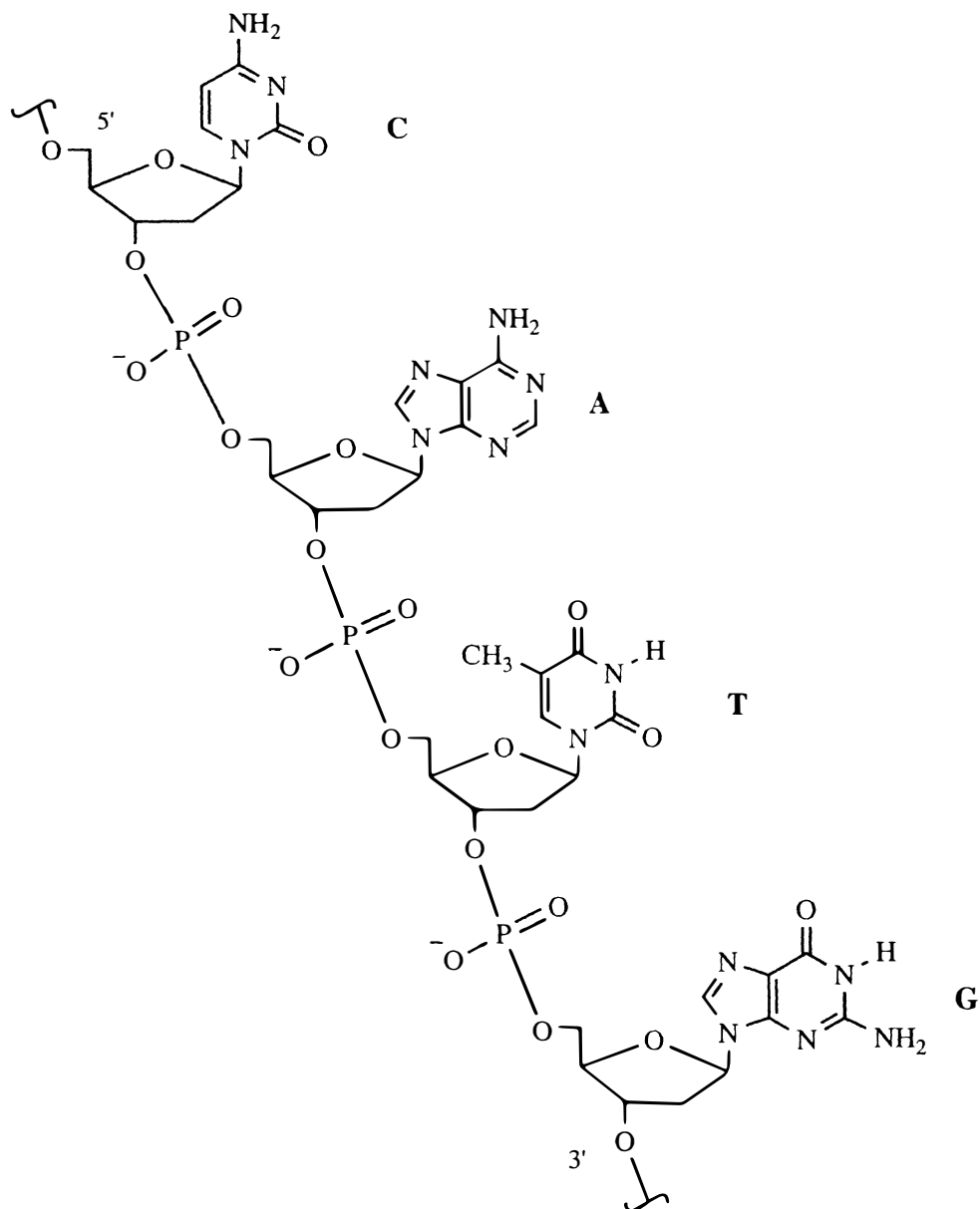


23-70





23-72 Bonds from C to H are omitted for simplicity.



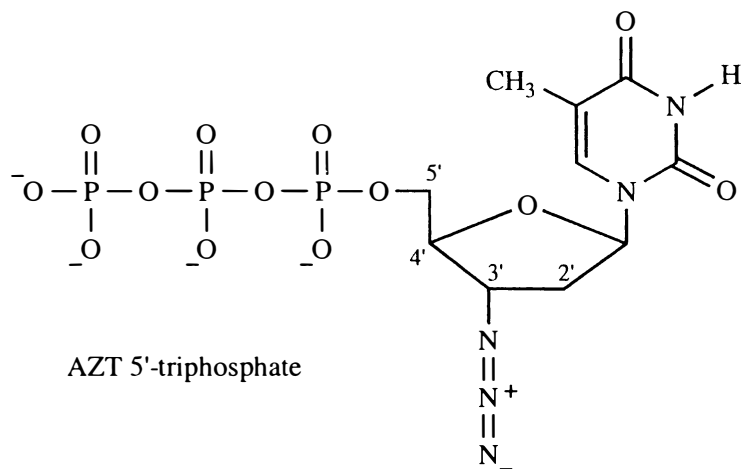
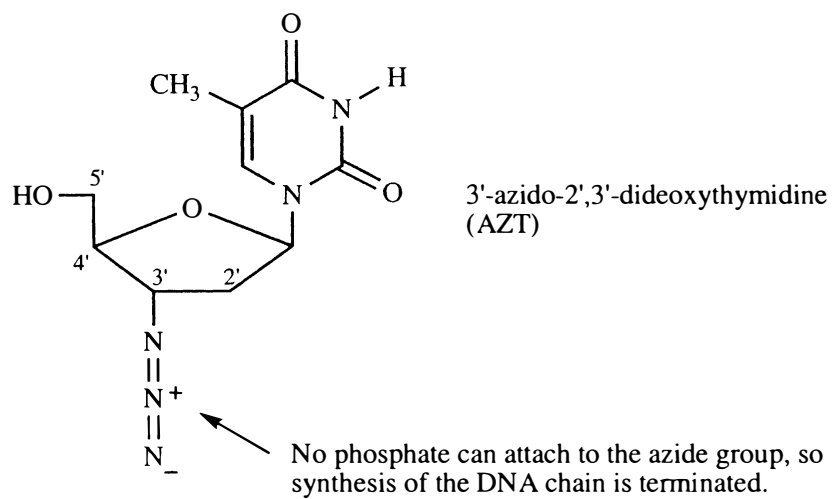
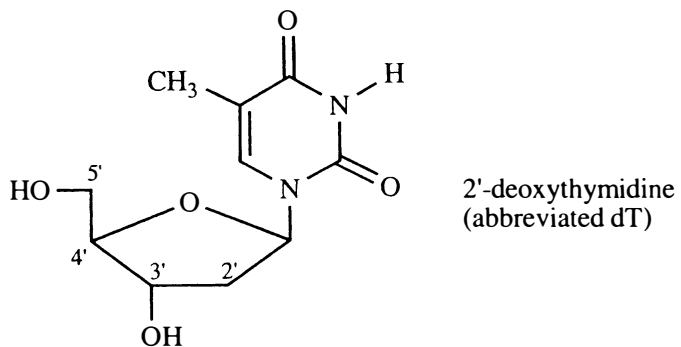
23-73

(a) No, there is no relation between the amount of G and A.

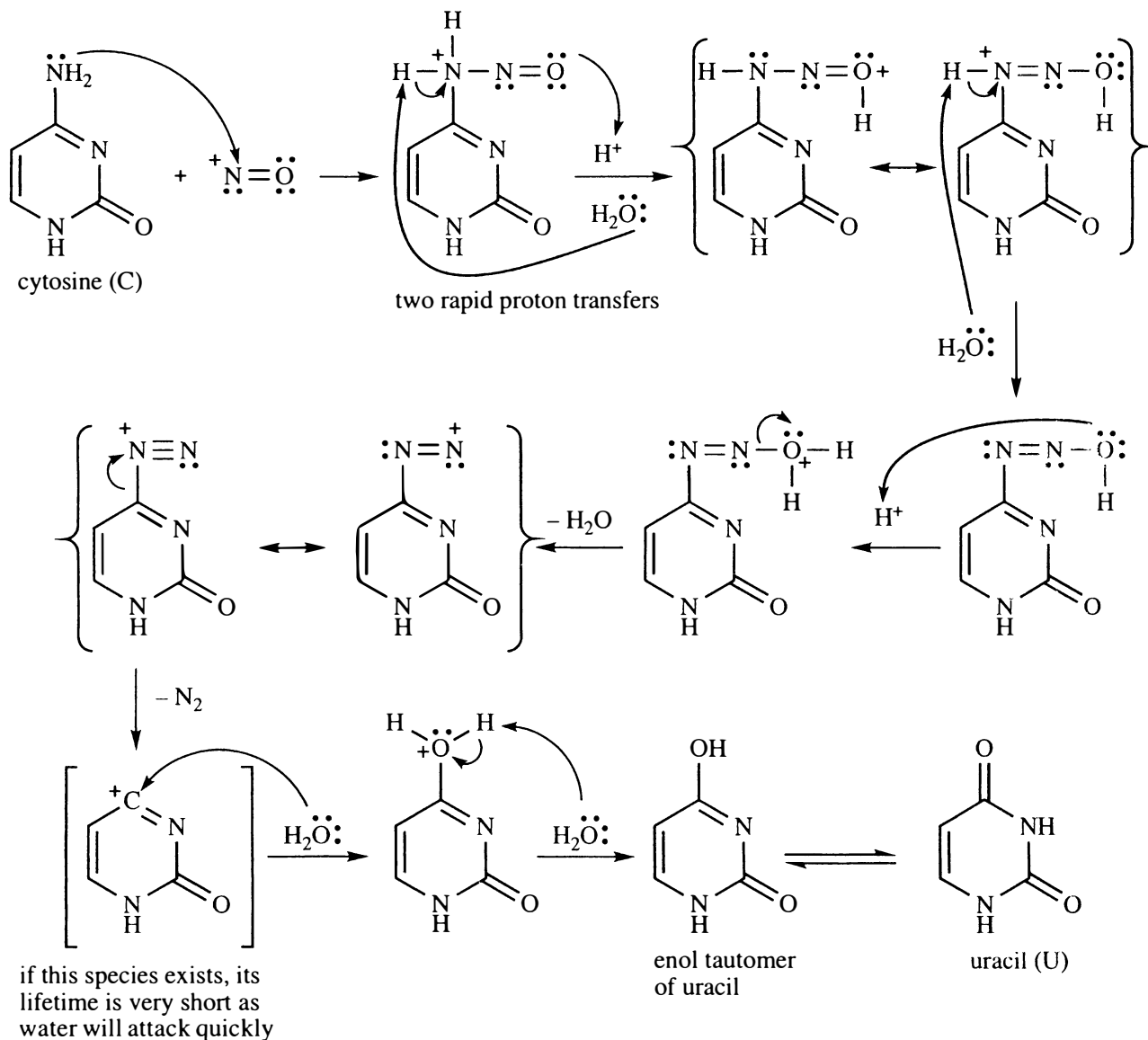
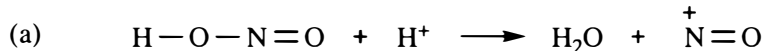
(b) Yes, this must be true mathematically.

(c) Chargaff's rule must apply only to double-stranded DNA. For each G in one strand, there is a complementary C in the opposing strand, but there is no correlation between G and C *in the same strand*.

23-74 Bonds from C to H are omitted for simplicity.



23-75 Recall from section 19-17 that nitrous acid is unstable, generating nitrosonium ion.

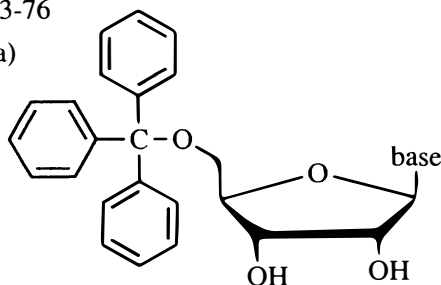


(b) In base pairing, cytosine pairs with guanine. If cytosine is converted to uracil, however, each replication will not carry the complement of cytosine (guanine) but instead will carry the complement of uracil (adenine). This is the definition of a mutation, where the wrong base is inserted in a nucleic acid chain.

(c) In RNA, the transformation of cytosine (C) to uracil (U) is not detected as a problem because U is a base normally found in RNA so it goes unrepaired. In DNA, however, thymine (with an extra methyl group) is used instead of uracil. If cytosine is diazotized to uracil, the DNA repair enzymes detect it as a mutation and correct it.

23-76

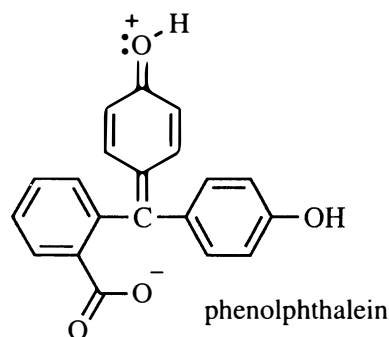
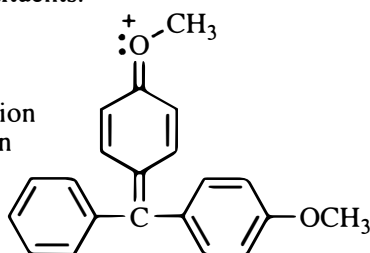
(a)



(b) Trityl groups are specific for 1° alcohols for steric reasons: the trityl group is so big that even a 2° alcohol is too crowded to react at the central carbon. It is possible for a trityl to go on a 2° alcohol, but the reaction is exceedingly slow and in the presence of a 1° alcohol, the reaction is done at the 1° alcohol long before the 2° alcohol gets started.

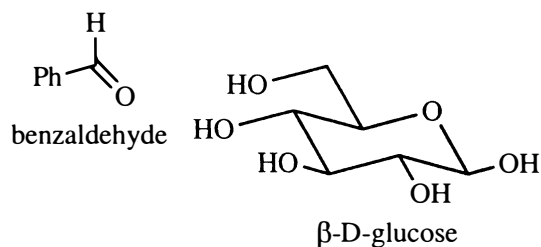
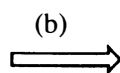
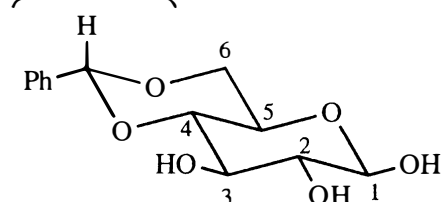
(c) Reactions happen faster when the product or intermediate is stabilized. Each OCH₃ group stabilizes the carbocation by resonance as shown here; two OCH₃ groups stabilize more than just one, increasing the rate of removal. The color comes from the extended conjugation through all three rings and out onto the OCH₃ groups. Compare the DMT structure with that of phenolphthalein, the most common acid base indicator, that turns pink in its ring open form shown here. Phenolphthalein is simply another trityl group with different substituents.

one of the major resonance contributors showing the delocalization of the positive charge on the oxygen



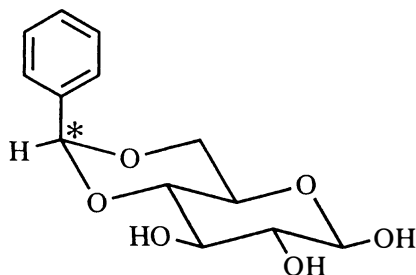
23-77

(a) acetal



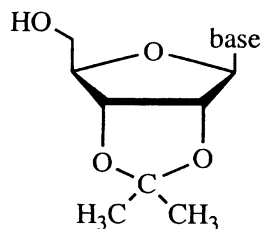
The 4- and 6-OH groups of glucose reacted with benzaldehyde to form the acetal.

(c)



(c) and (d) The chiral center is marked with (*). This stereoisomer is a diastereomer since only one chiral center is inverted. This diastereomer puts the phenyl group in an axial position, definitely less stable than the structure shown in part (a). Only the product shown in (a) will be isolated from this reaction.

(e)

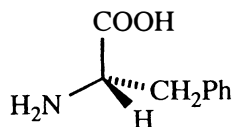


Only the 2'- and 3'-OH groups are close enough to form this cyclic acetal (ketal) from acetone, called an acetonide.

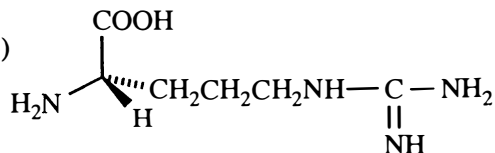
CHAPTER 24—AMINO ACIDS, PEPTIDES, AND PROTEINS

24-1

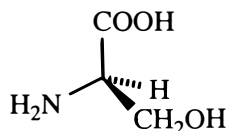
(a)



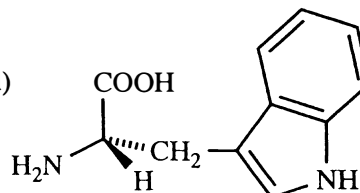
(b)



(c)



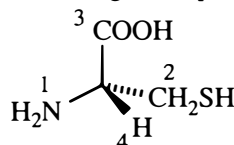
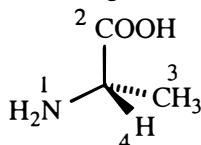
(d)



24-2

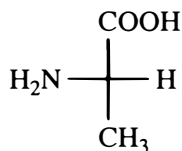
(a) The configurations around the asymmetric carbons of (*R*)-cysteine and (*S*)-alanine are the same. The *designation* of configuration changes because sulfur changes the priorities of the side chain and the COOH.

(*S*)-alanine with
group priorities shown

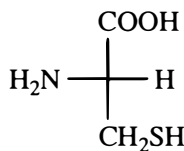


(*R*)-cysteine with group priorities shown; note that the COOH and the CH₂SH priorities are reversed compared with (*S*)-alanine

(b) Fischer projections show that both (*S*)-alanine and (*R*)-cysteine are L-amino acids.



(*S*)-alanine
L-alanine

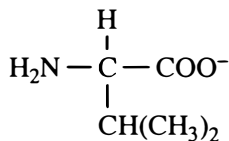


(*R*)-cysteine
L-cysteine

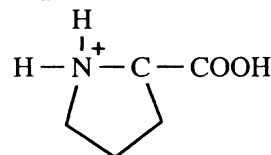
24-3 In their evolution, plants have needed to be more resourceful than animals in developing biochemical mechanisms for survival. Thus, plants make more of their own required compounds than animals do. The amino acid phenylalanine is produced by plants but required in the diet of mammals. To interfere with a plant's production of phenylalanine is fatal to the plant, but since humans do not produce phenylalanine, glyphosate is virtually non-toxic to us.

24-4 Here is a simple way of determining if a group will be protonated: *at solution pH below the group's pK_a value, the group will be protonated; at pH higher than the group's pK_a value, it will not be protonated.*

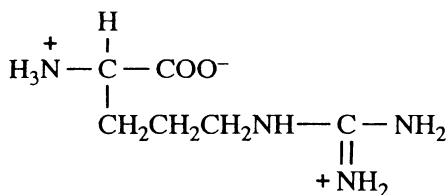
(a)



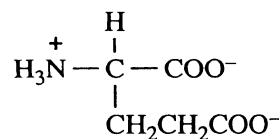
(b)



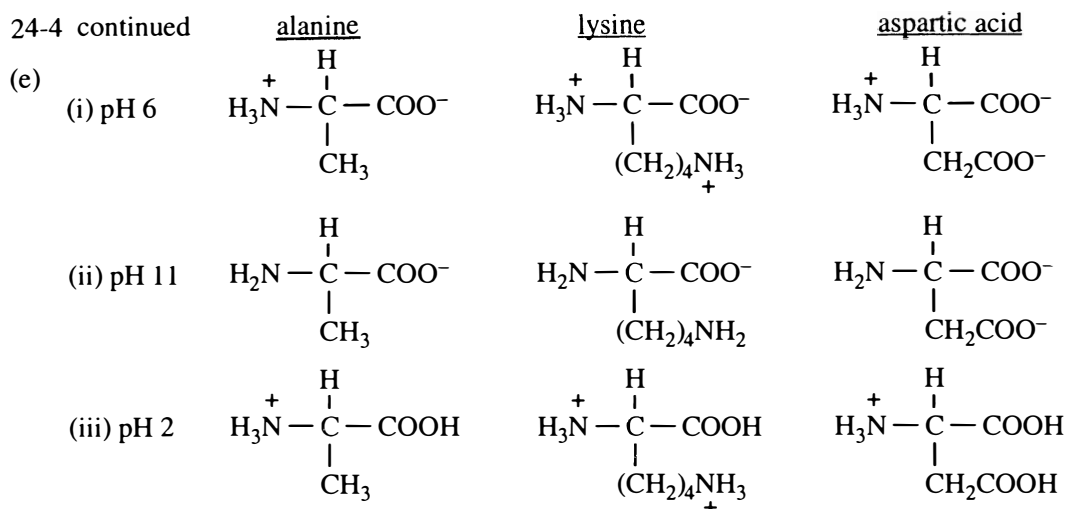
(c)



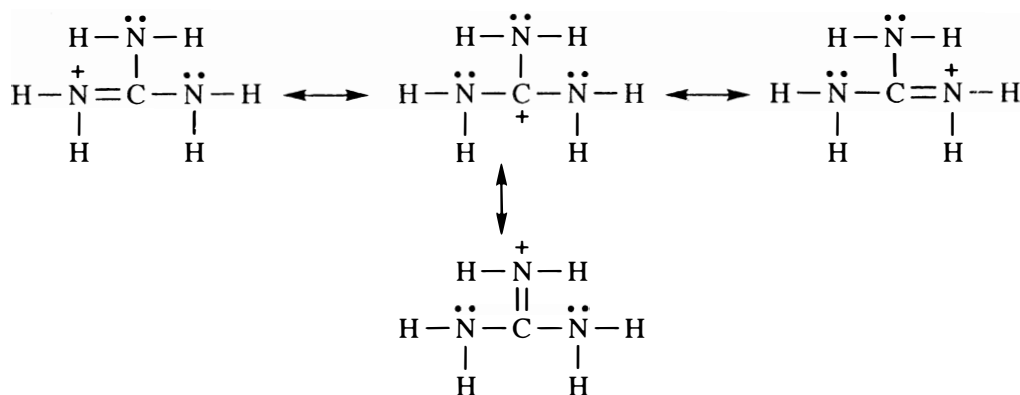
(d)



24-4 continued

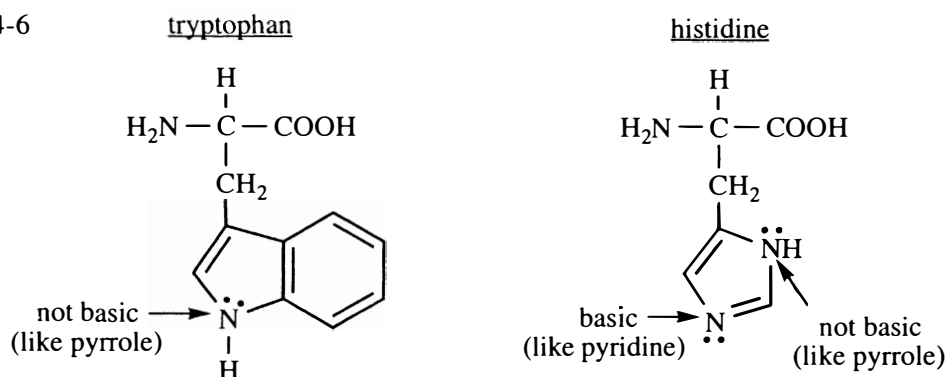


24-5



Protonation of the guanidino group gives a resonance-stabilized cation with all octets filled and the positive charge delocalized over three nitrogen atoms. Arginine's strongly basic isoelectric point reflects the unusual basicity of the guanidino group due to this resonance stabilization in the protonated form. (See Problems 1-39 and 19-49(a).)

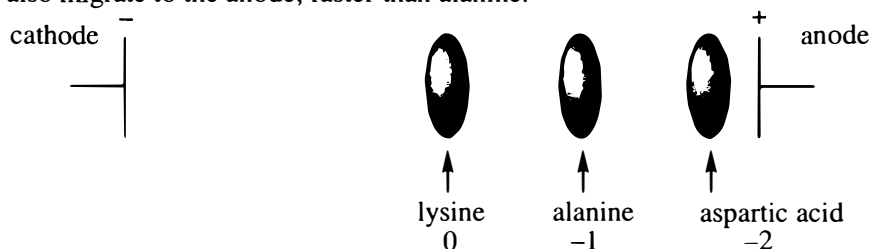
24-6



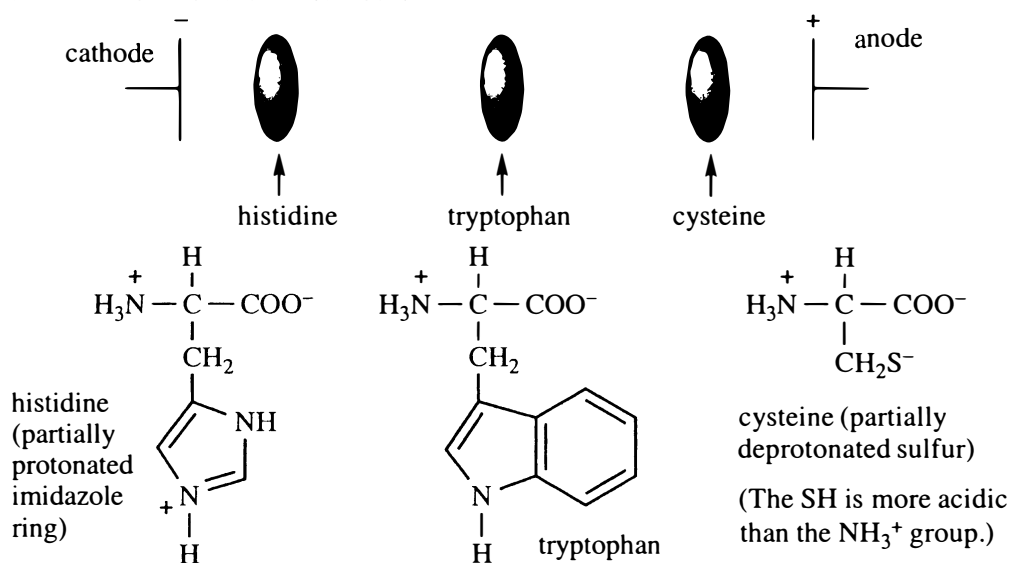
The basicity of any nitrogen depends on its electron pair's availability for bonding with a proton. In tryptophan, the nitrogen's electron pair is part of the aromatic π system; without this electron pair in the π system, the molecule would not be aromatic. Using this electron pair for bonding to a proton would therefore destroy the aromaticity—not a favorable process.

In the imidazole ring of histidine, the electron pair of one nitrogen is also part of the aromatic π system and is unavailable for bonding; this nitrogen is not basic. The electron pair on the other nitrogen, however, is in an sp^2 orbital available for bonding, and is about as basic as pyridine.

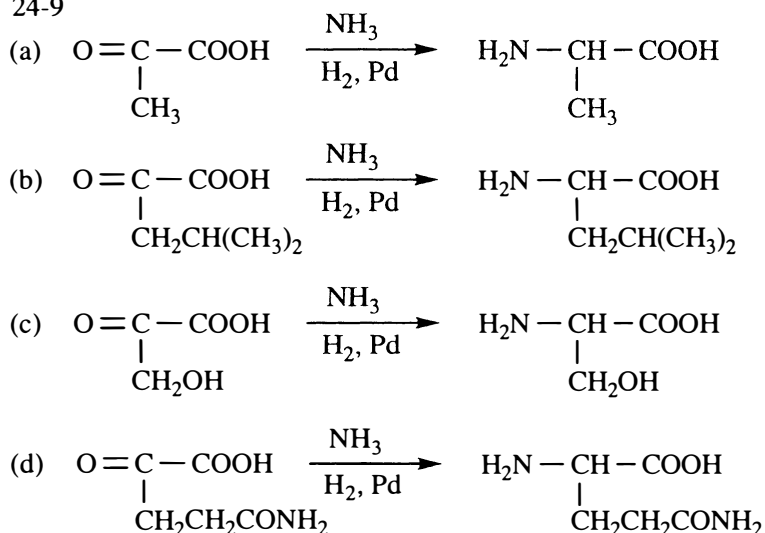
24-7 At pH 9.7, alanine (isoelectric point (IEP) 6.0) has a charge of -1 and will migrate to the anode. Lysine (IEP 9.7) is at its isoelectric point and will not move. Aspartic acid (IEP 2.8) has a charge of -2 and will also migrate to the anode, faster than alanine.



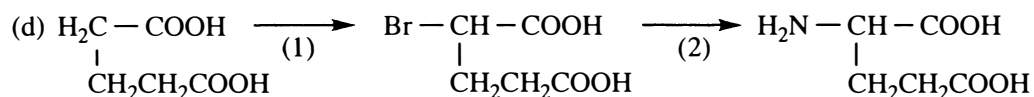
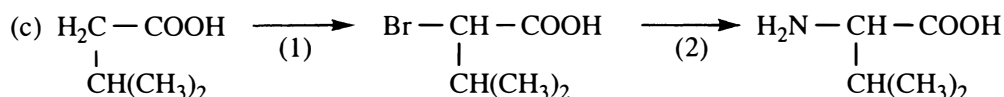
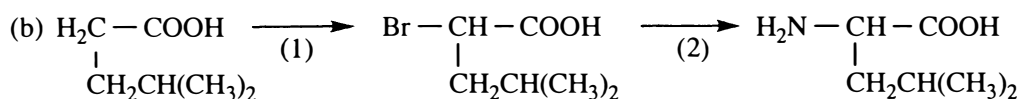
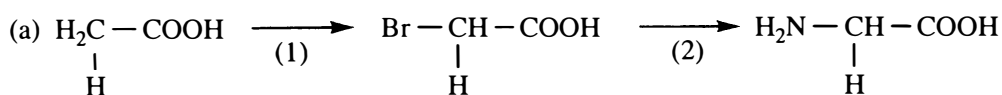
24-8 At pH 6.0, tryptophan (IEP 5.9) has a charge of zero and will not migrate. Cysteine (IEP 5.0) has a partial negative charge and will move toward the anode. Histidine (IEP 7.6) has a partial positive charge and will move toward the cathode.



24-9

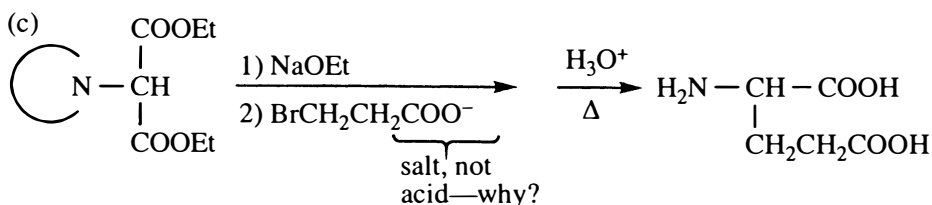
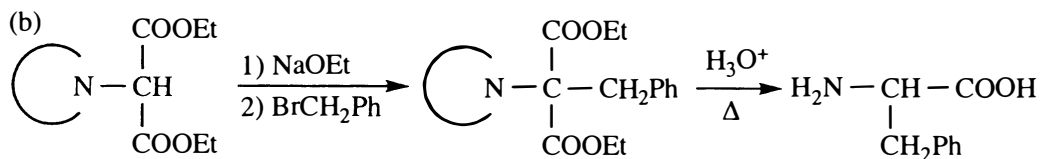
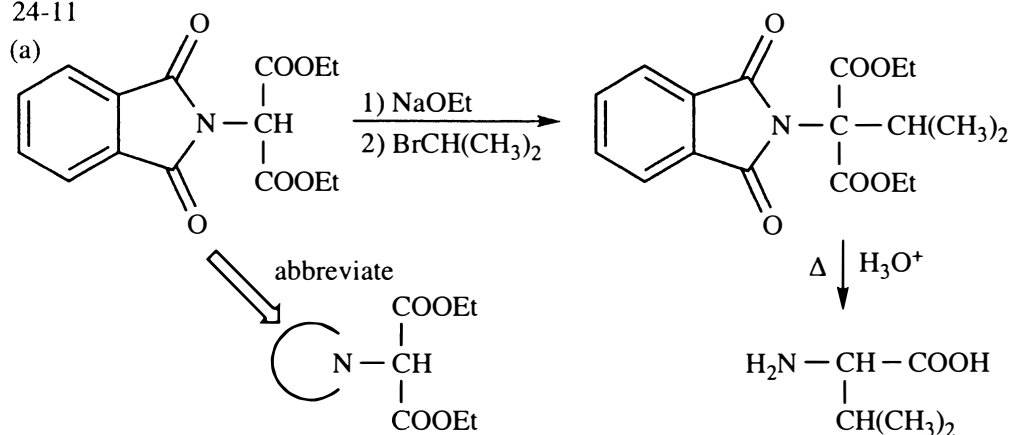


24-10 All of these reactions use: first arrow: (1) Br_2/PBr_3 , followed by H_2O workup; second arrow: (2) excess NH_3 , followed by neutralizing workup.

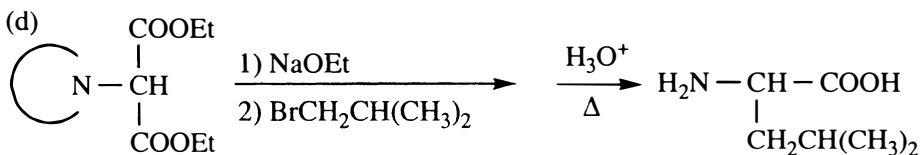


In part (d), care must be taken to avoid reaction α to the other COOH . In practice, this would be accomplished by using less than one-half mole of bromine per mole of the diacid.

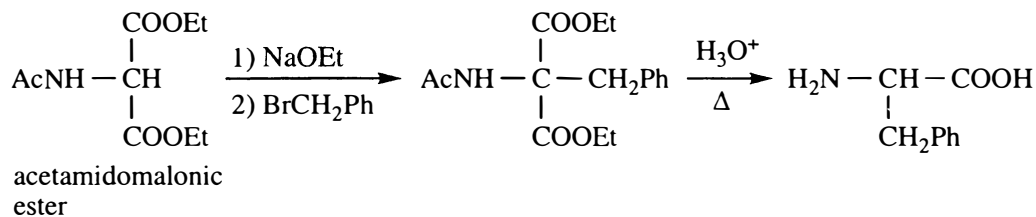
24-11



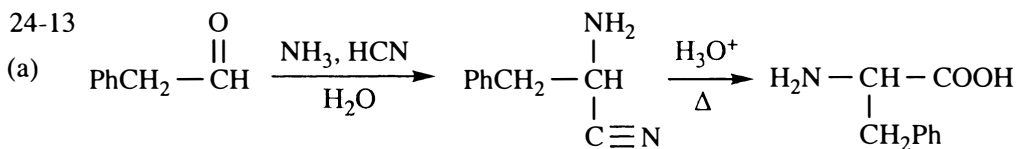
24-11 continued



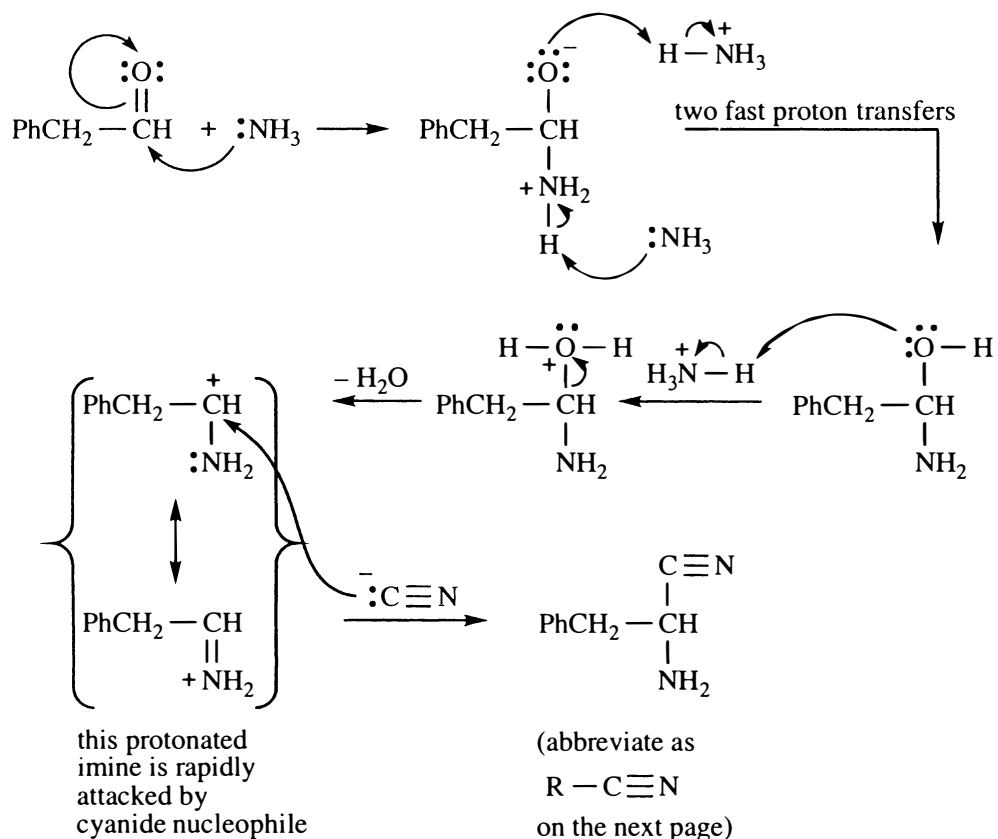
24-12



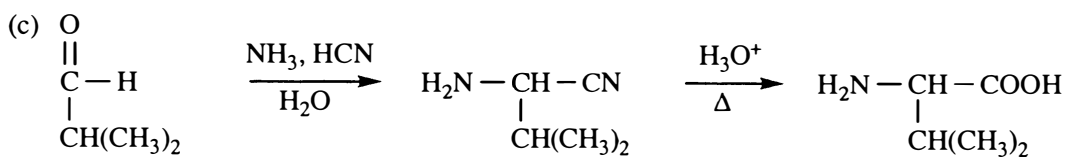
24-13



(b) While the solvent for the Strecker synthesis is water, the proton acceptor is ammonia and the proton donor is ammonium ion.

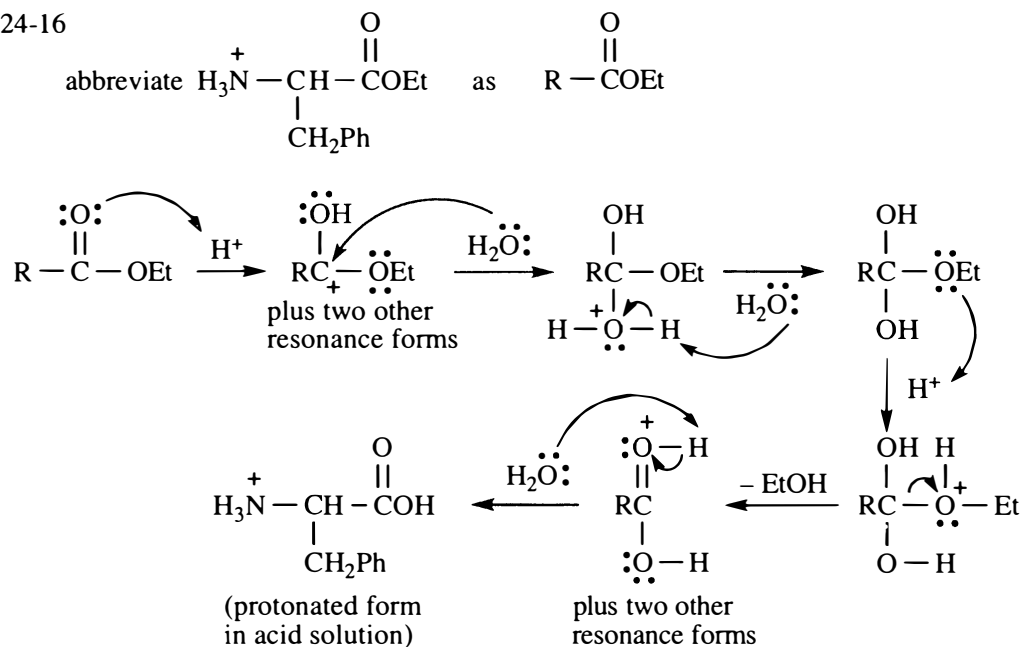


mechanism of acid hydrolysis of the nitrile

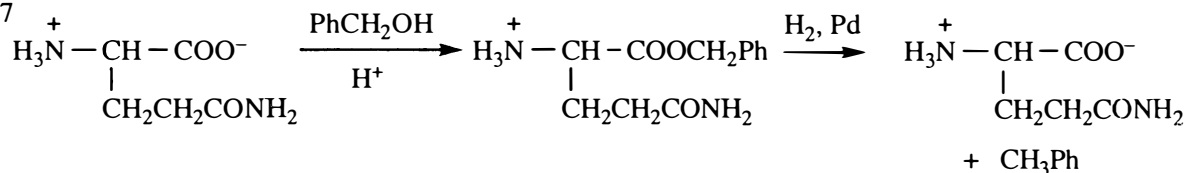


24-15 In acid solution, the free amino acid will be protonated, with a positive charge, and probably soluble in water as are other organic ions. The acylated amino acid, however, is not basic since the nitrogen is present as an amide. In acid solution, the acylated amino acid is neutral and not soluble in water. Water extraction or ion-exchange chromatography (Figure 24-11) would be practical techniques to separate these compounds.

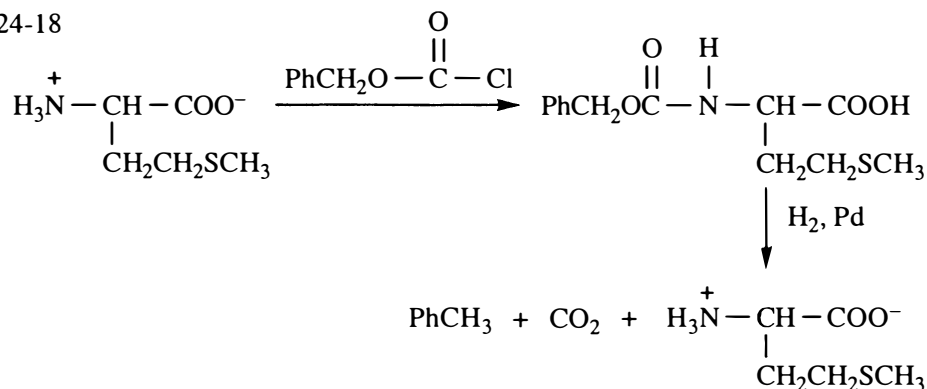
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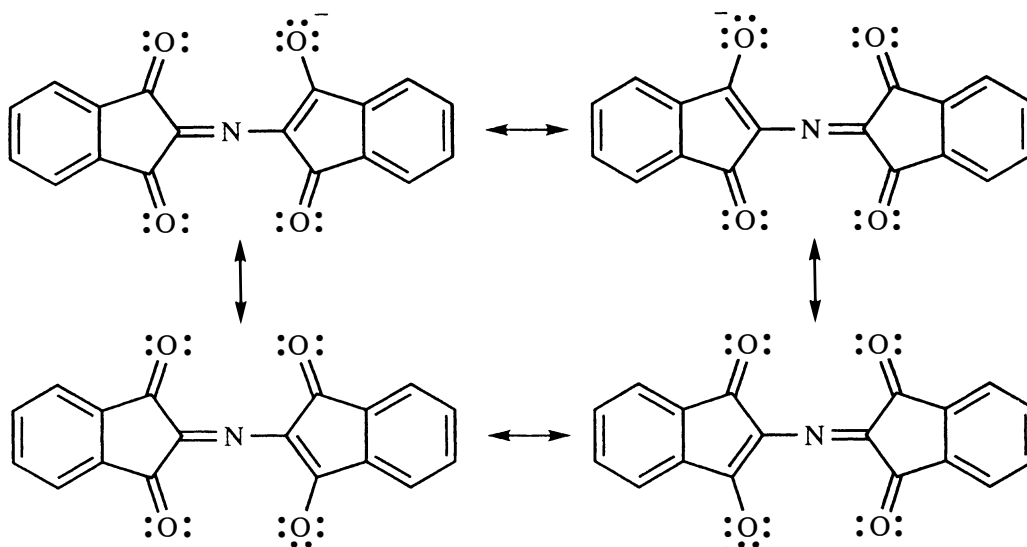
24-17



24-18

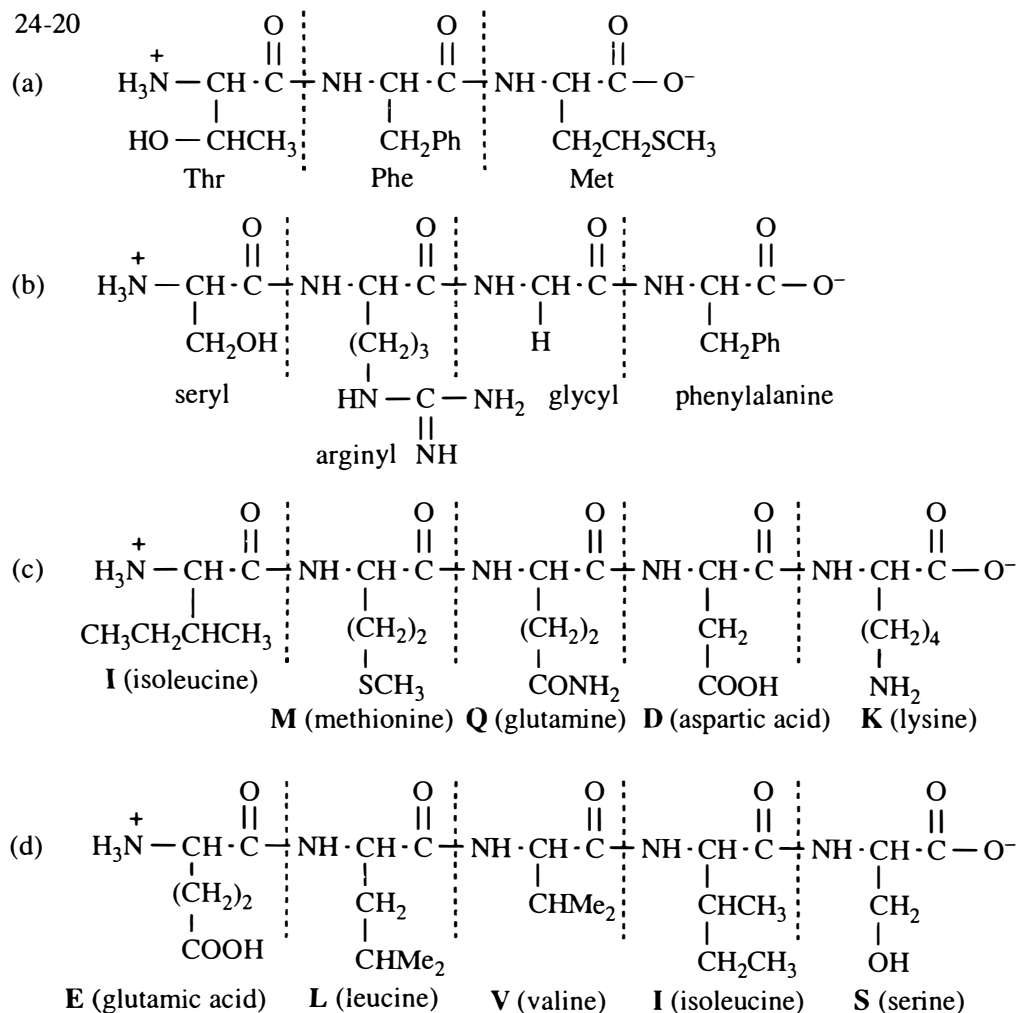


24-19

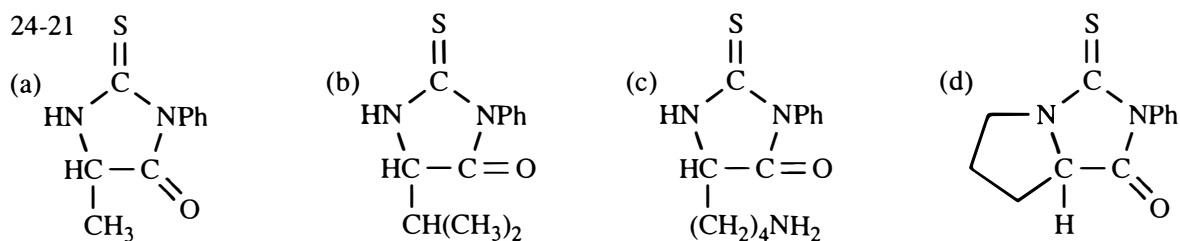


These are the most significant resonance contributors in which the electronegative oxygens carry the negative charge. There are also two other forms in which the negative charge is on the carbons bonded to the nitrogen, plus the usual resonance forms involving the alternate Kekulé structures of the benzene rings.

24-20

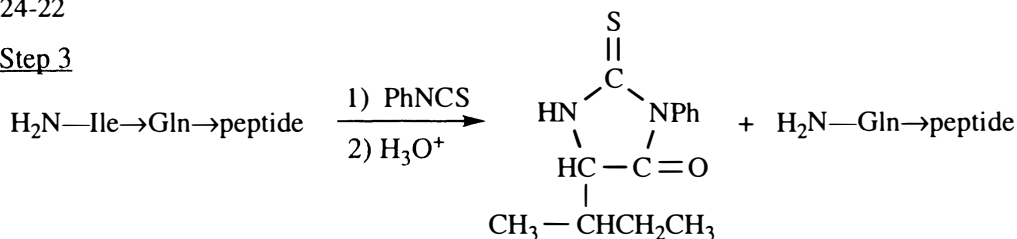


Try spelling your name in peptides!

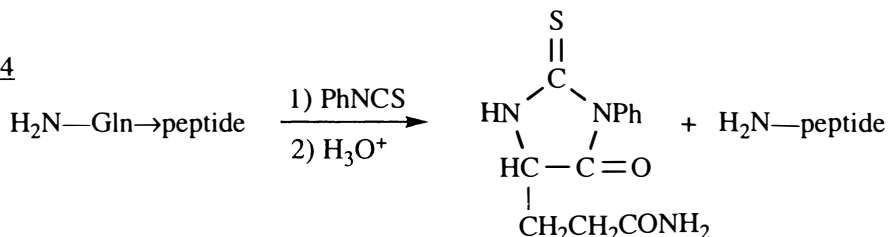


24-22

Step 3

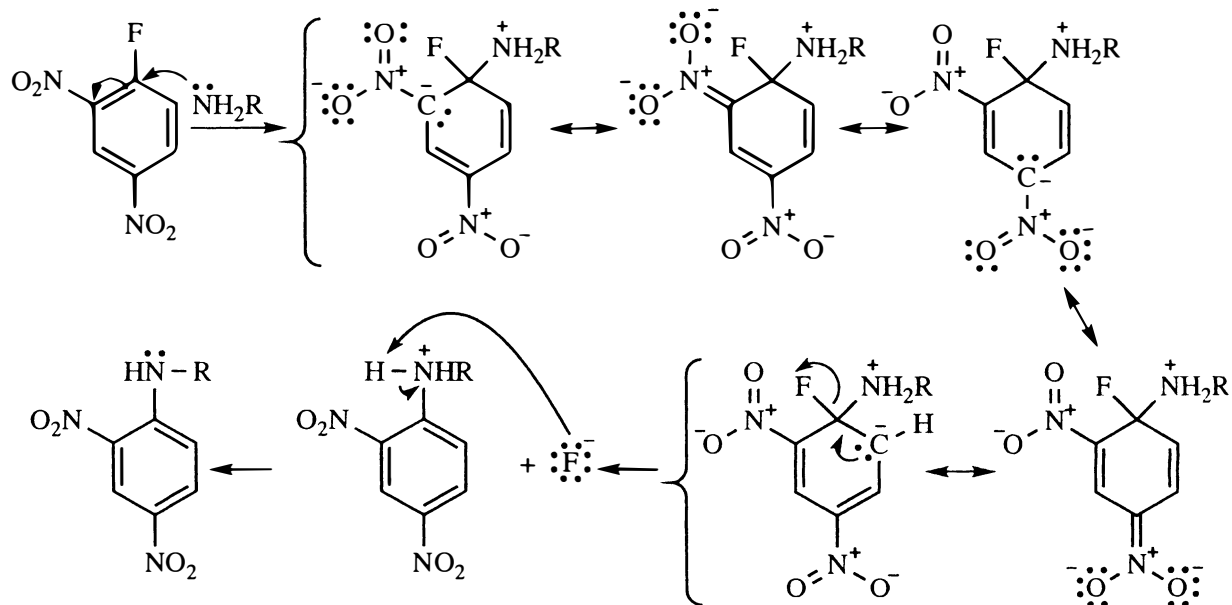


Step 4



24-23 Abbreviate the N-terminus of the peptide chain as NH_2R .

(a) This is a nucleophilic aromatic substitution by the addition-elimination mechanism. The presence of two nitro groups makes this reaction feasible under mild conditions.



(b) The main drawback of the Sanger method is that only one amino acid is analyzed per sample of protein. The Edman degradation can usually analyze more than 20 amino acids per sample of protein.

24-24

Diagram illustrating the relationship between trypsin and chymotrypsin in the digestion of a protein.

The protein sequence is: Tyr-Ile-Gln-Arg-Leu-Gly-Phe-Lys-Asn-Trp-Phe-Gly-Ala-Lys-Gly-Gln-Gln-NH₂.

Trypsin cleaves the protein at the C-terminal of Arg, Lys, and Asn.

Chymotrypsin cleaves the protein at the C-terminal of Tyr, Phe, and Trp.

The diagram shows the protein sequence with arrows indicating the cleavage sites for both enzymes. Trypsin cleaves at the C-terminal of Arg, Lys, and Asn. Chymotrypsin cleaves at the C-terminal of Tyr, Phe, and Trp.

Diagram illustrating the synthesis of a polypeptide chain using the growing chain method:

Initial fragments:

- Phe—Gln—Asn
- Pro—Arg—Gly•NH₂
- Cys—Tyr—Phe
- Asn—Cys—Pro—Arg

Intermediate step (indicated by a bracket):

Tyr—Phe—Gln—Asn

Final polypeptide chain (indicated by a bracket):

Cys—Tyr—Phe—Gln—Asn—Cys—Pro—Arg—Gly•NH₂

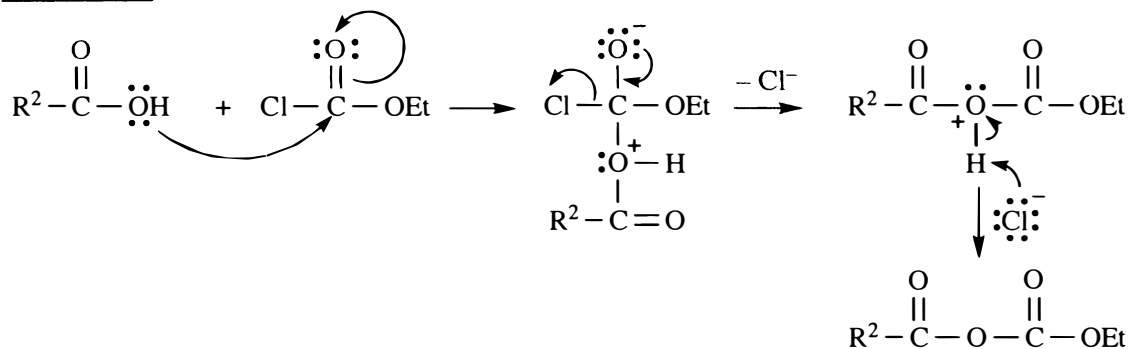
$$\begin{array}{ccc} \text{H}_2\text{N}-\text{CH}-\text{COOH} & \text{PhCH}_2\text{OC}-\text{NH}-\text{CH}-\text{COOH} & \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ | & \text{O} & | \\ \text{R}^1 & || & \text{R}^2 \\ \text{CH}_3 & & \text{CH}_3 \end{array}$$

$$\begin{array}{c}
 \text{PhCH}_2\text{O}-\text{C}(=\text{O})-\text{Cl} + \text{H}_2\text{N}-\text{R}^1 \longrightarrow \text{PhCH}_2\text{O}-\text{C}(\text{O}^-)(\text{Cl})-\text{NH}_2^+\text{R}^1 \\
 \downarrow \\
 \text{R}^2-\text{COOH} \leftarrow \text{PhCH}_2\text{O}-\text{C}(=\text{O})-\text{NH}-\text{R}^1 \leftarrow \text{Cl}^- + \text{PhCH}_2\text{O}-\text{C}(=\text{O})-\text{NH}_2^+\text{R}^1
 \end{array}$$

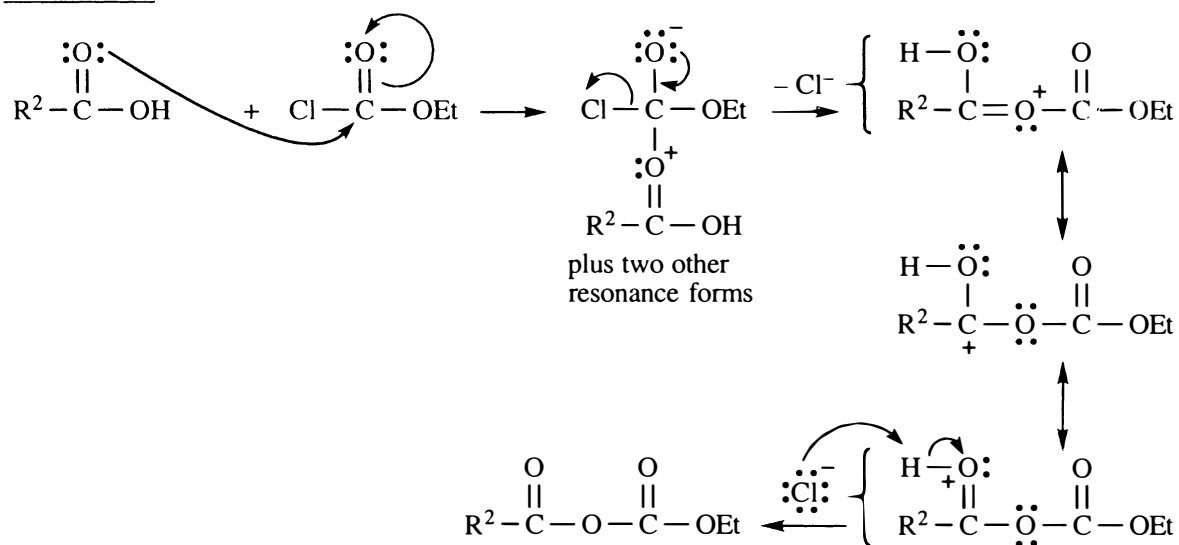
24-26 continued

two possible mechanisms of ethyl chloroformate activation

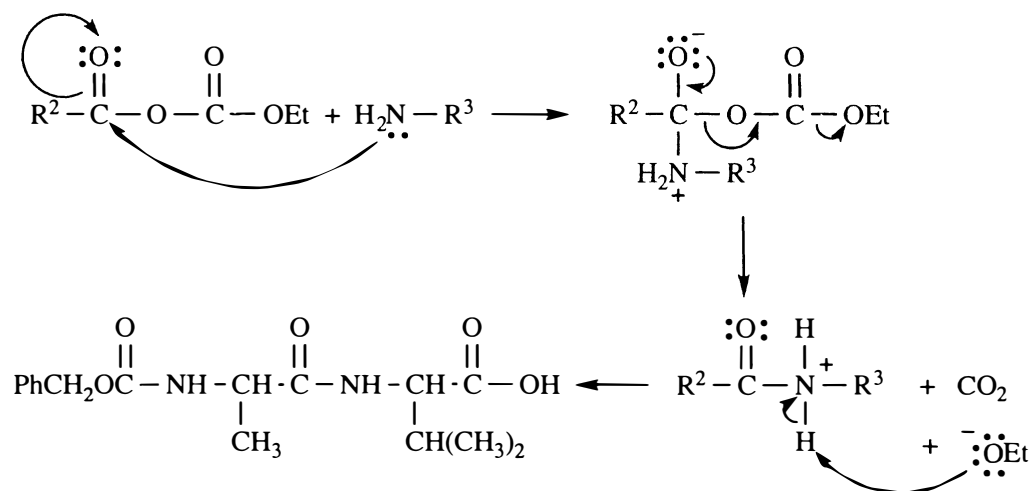
mechanism 1



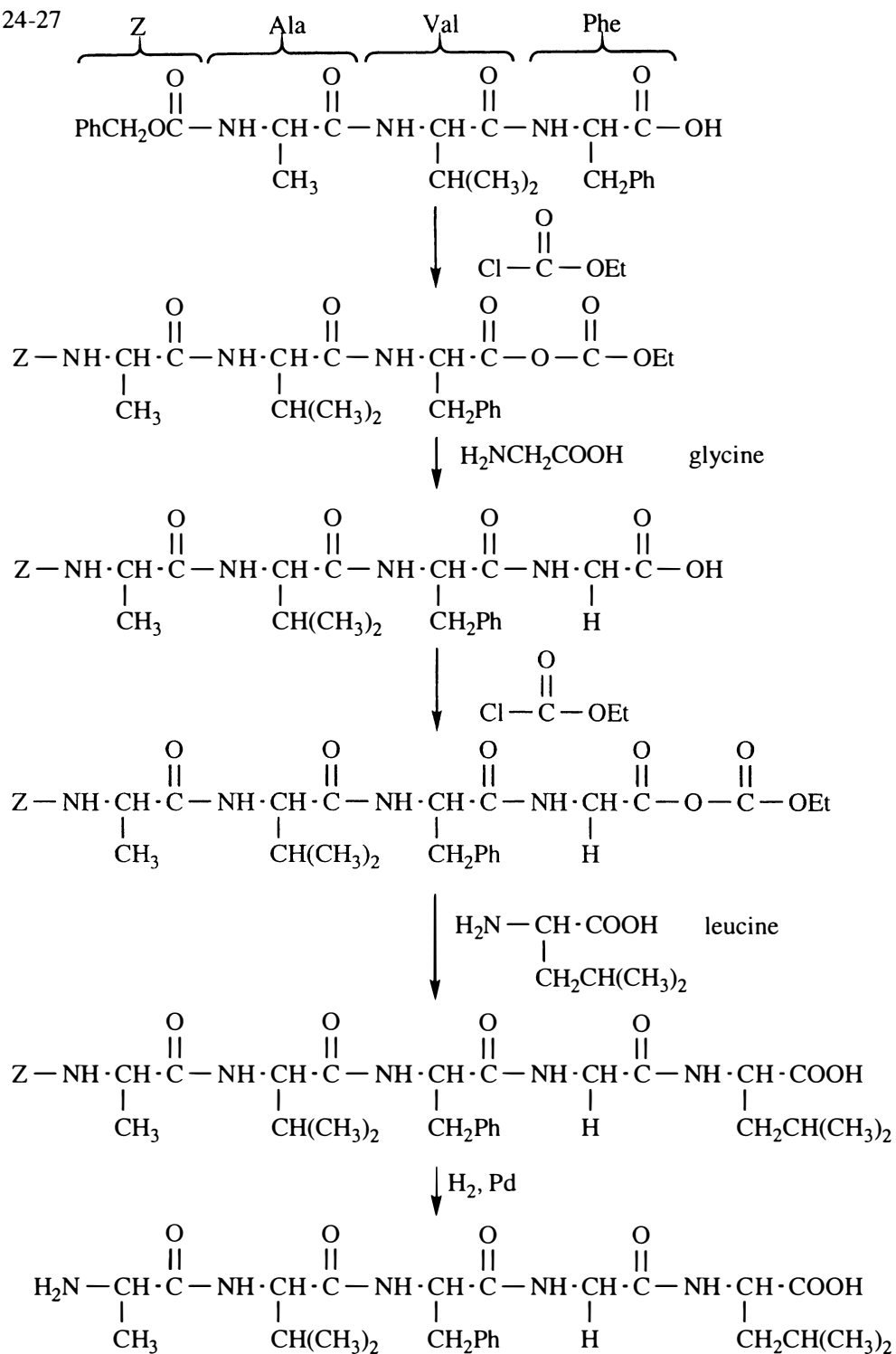
mechanism 2



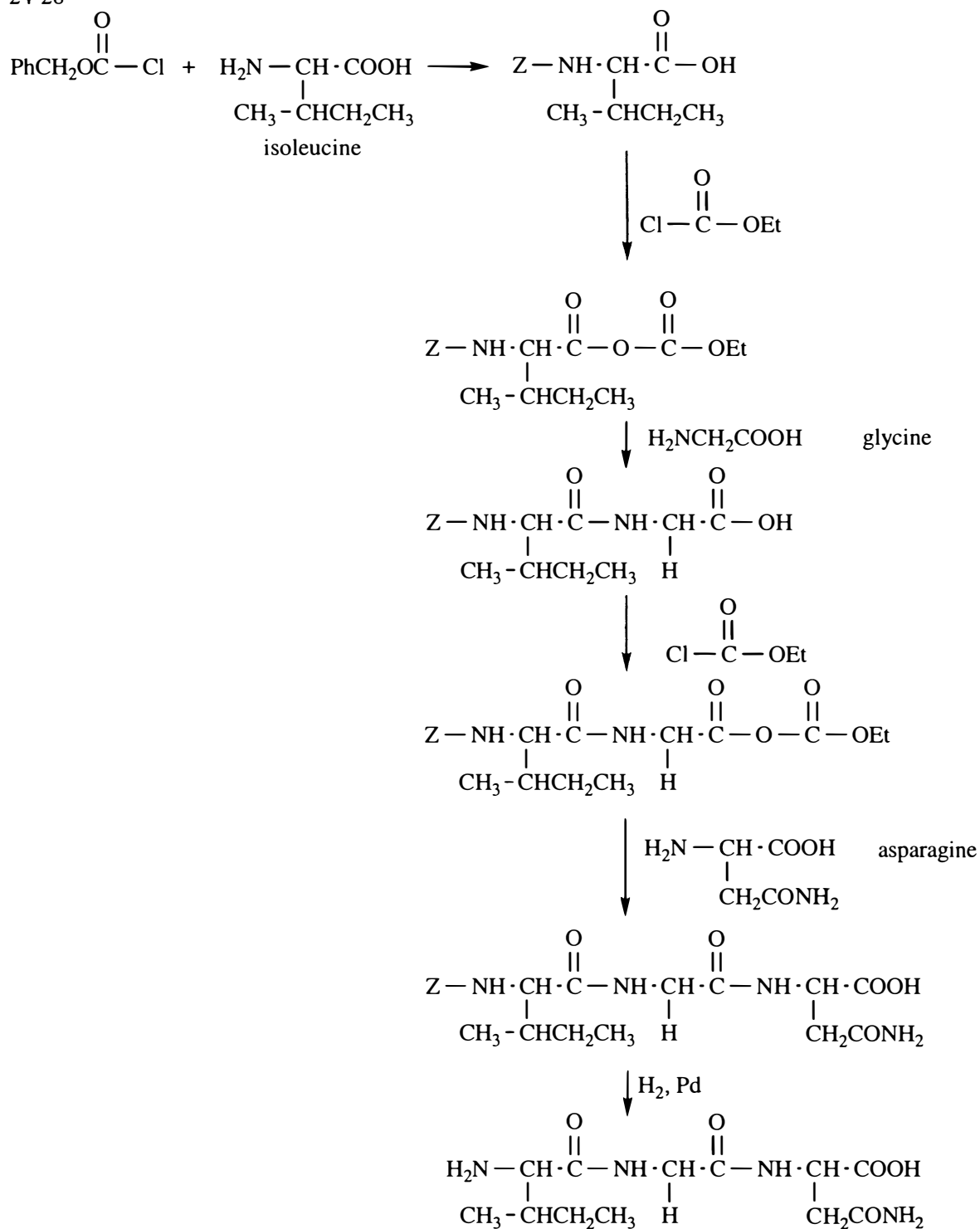
mechanism of the coupling with valine



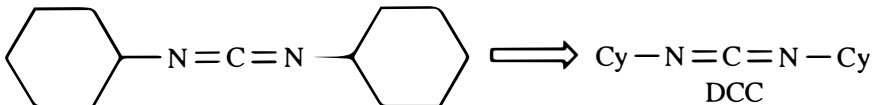
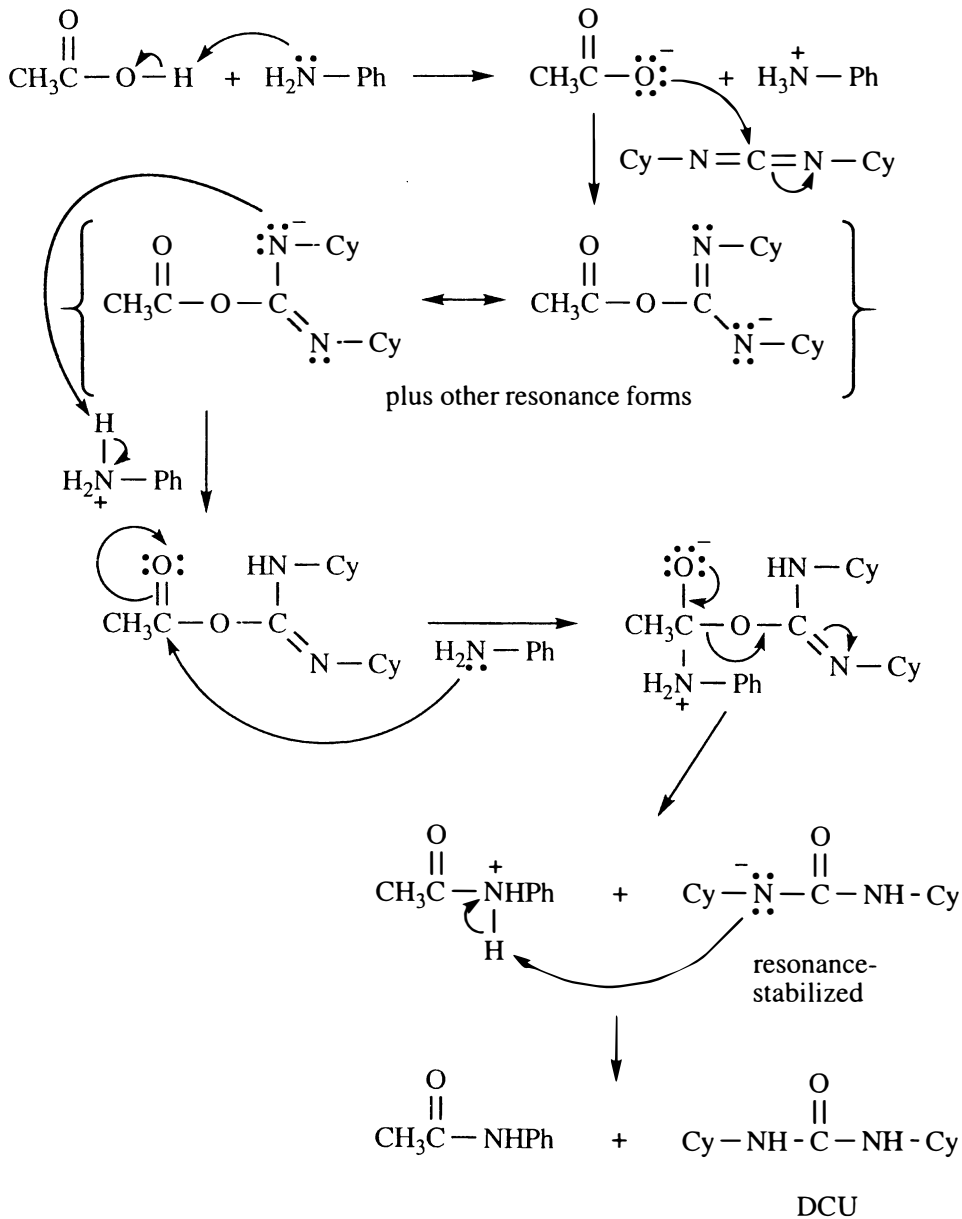
24-27

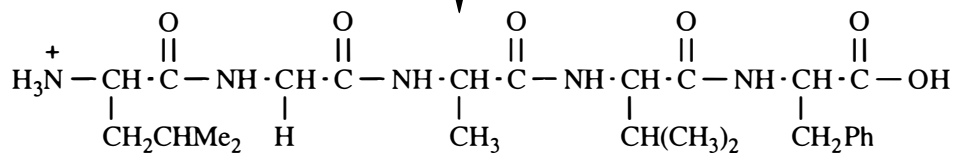
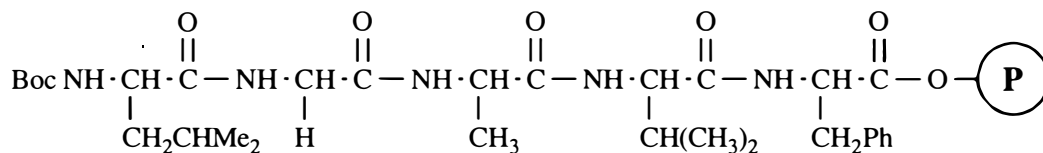
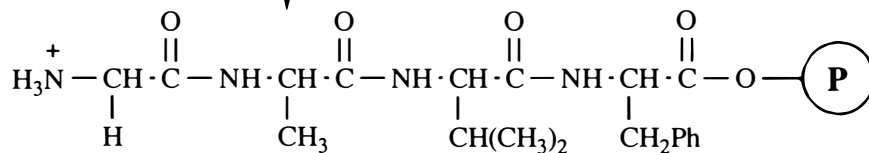
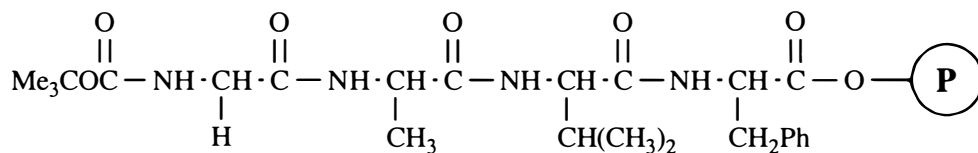
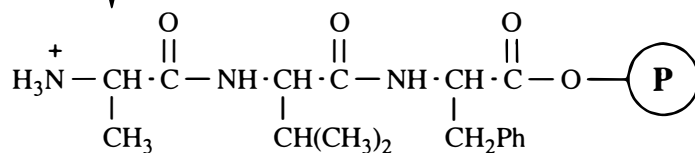


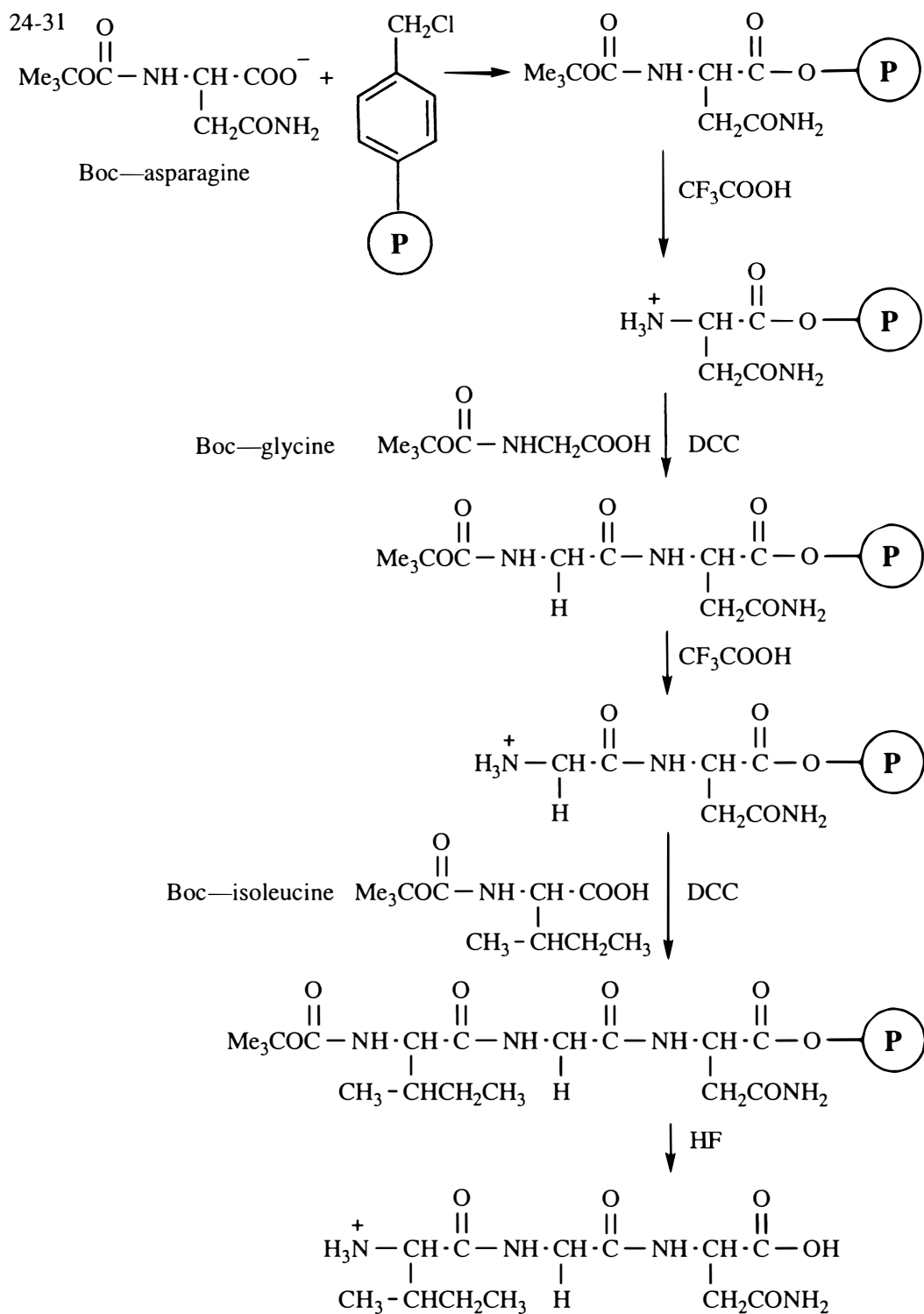
24-28



24-29 In this problem, "Cy" stands for "cyclohexyl".

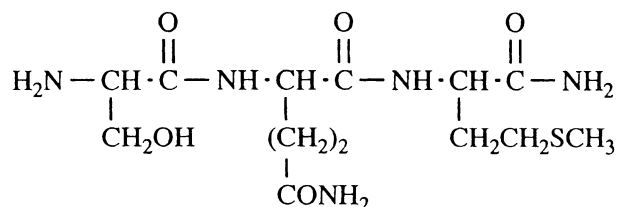
mechanism



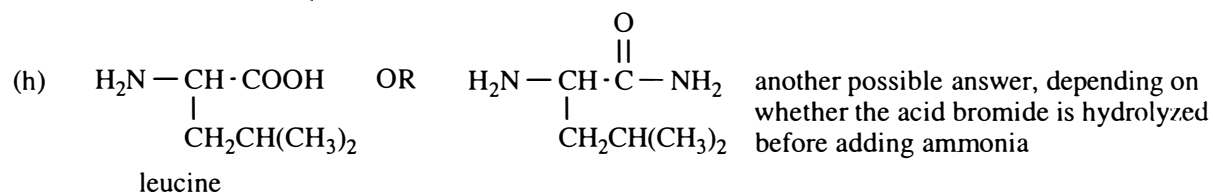
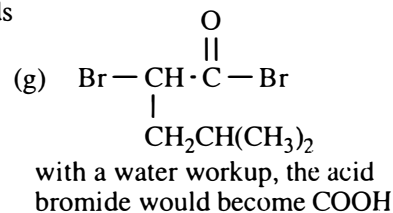
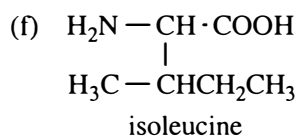
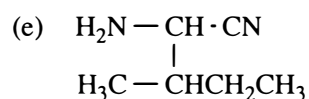
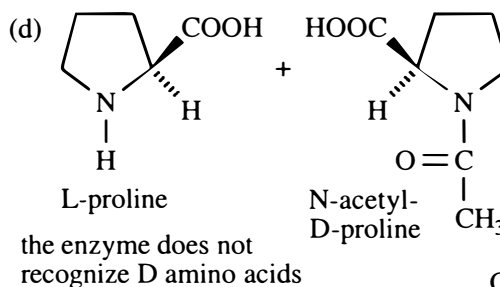
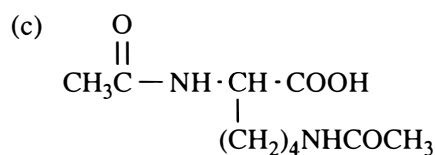
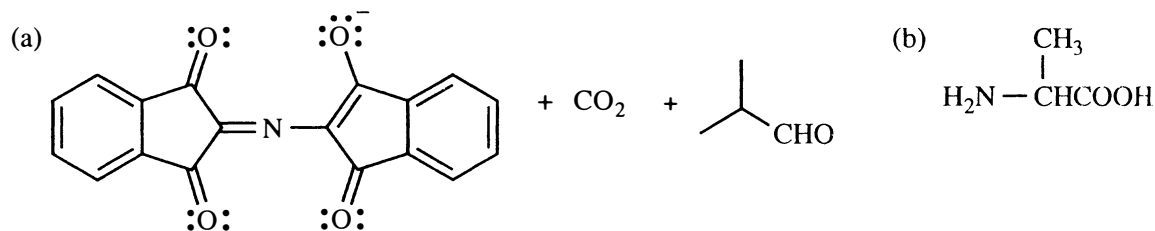


24-32 Please refer to solution 1-20, page 12 of this Solutions Manual.

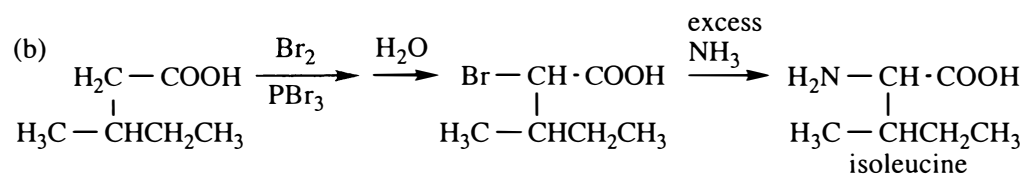
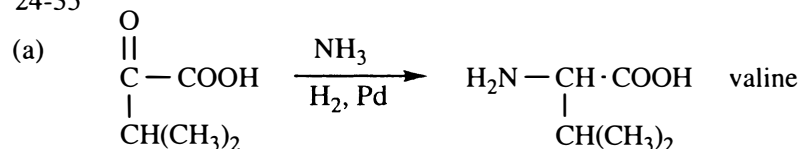
24-33



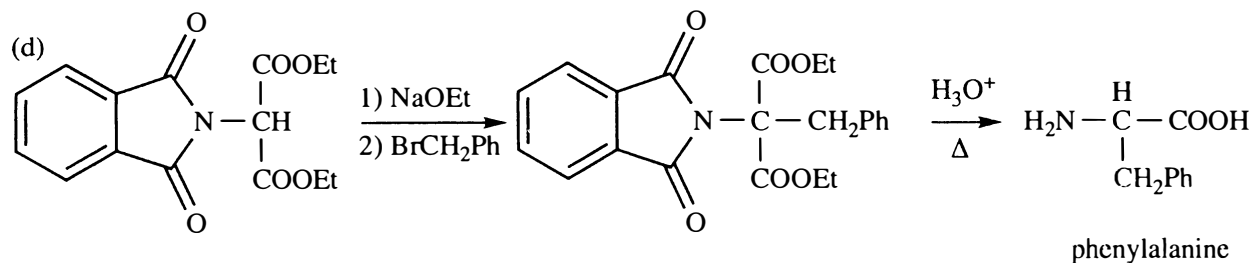
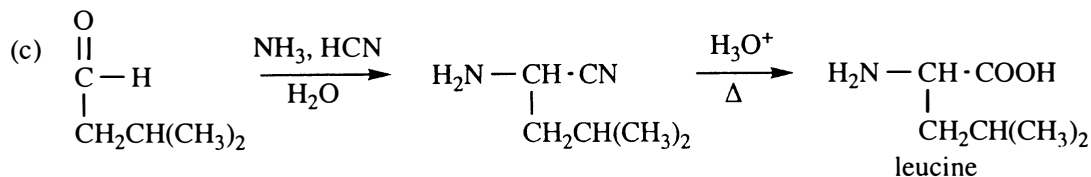
24-34



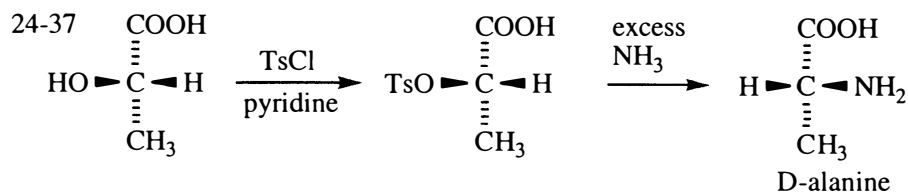
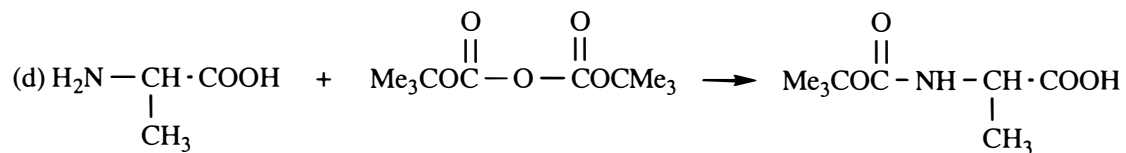
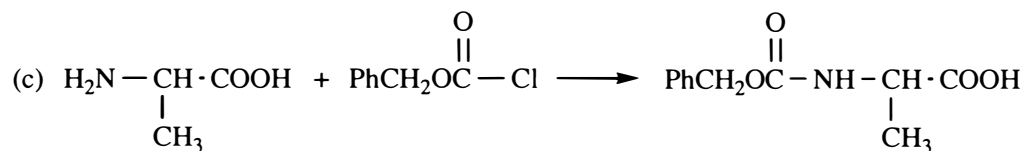
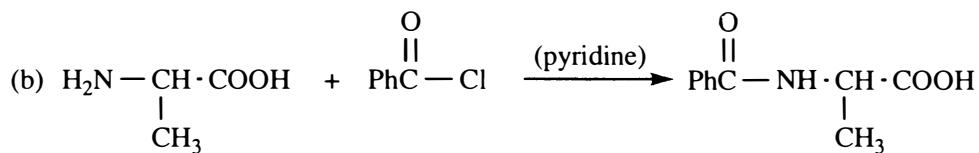
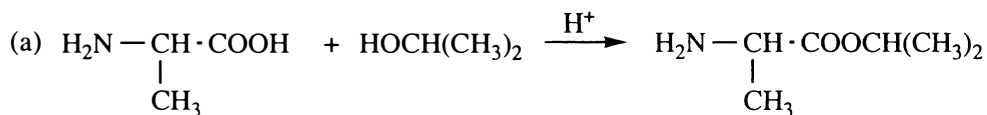
24-35

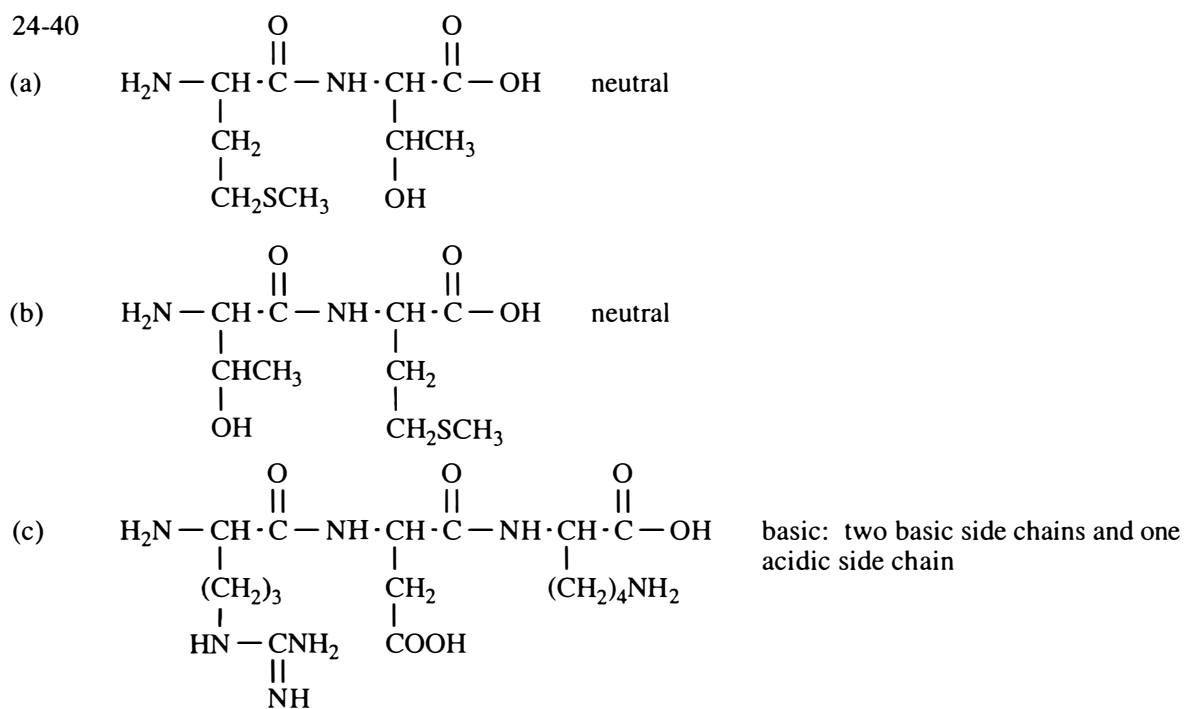
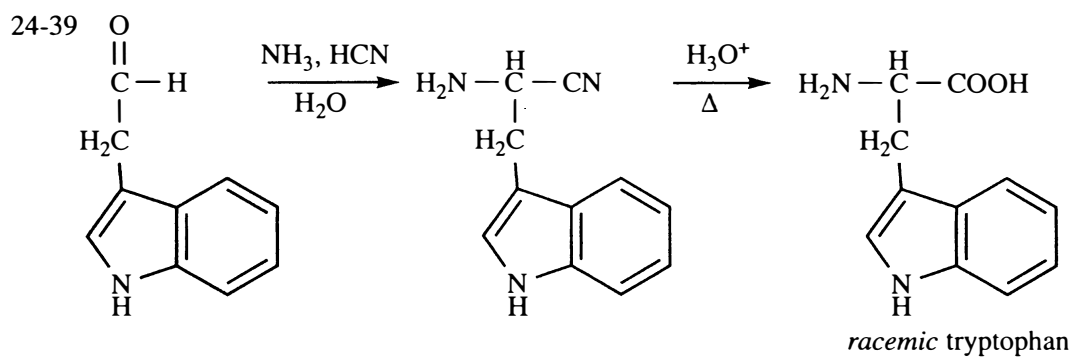
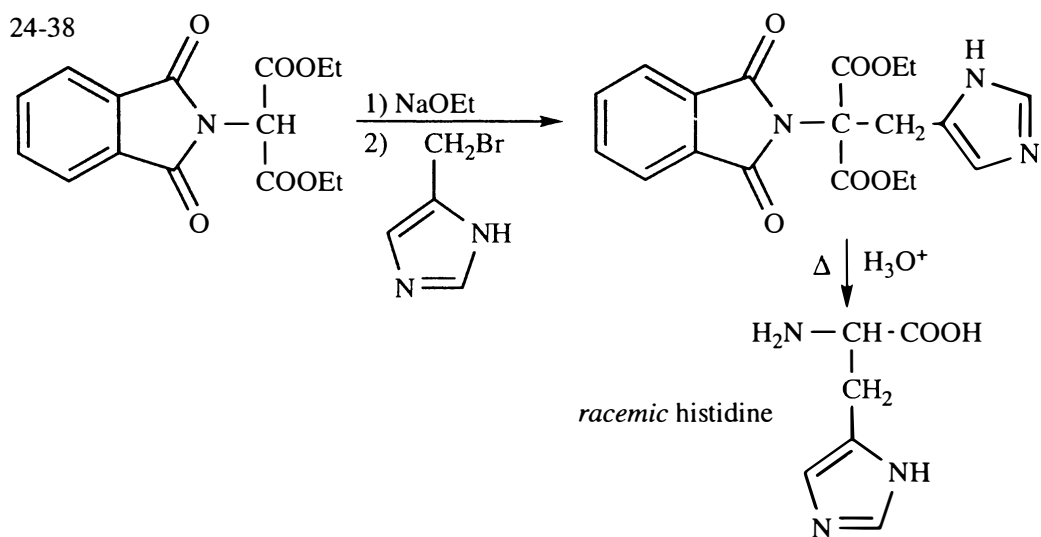


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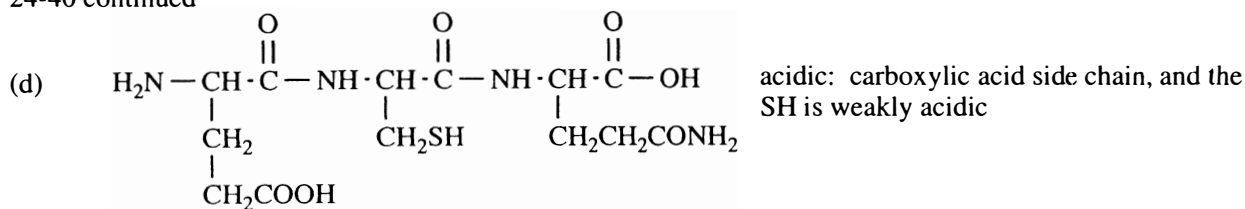


24-36

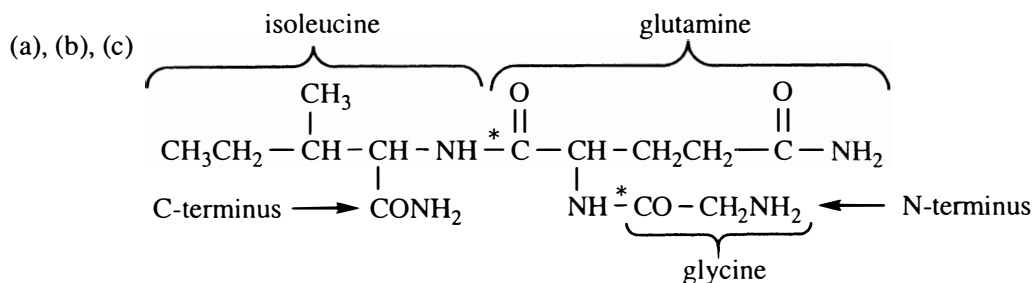




24-40 continued

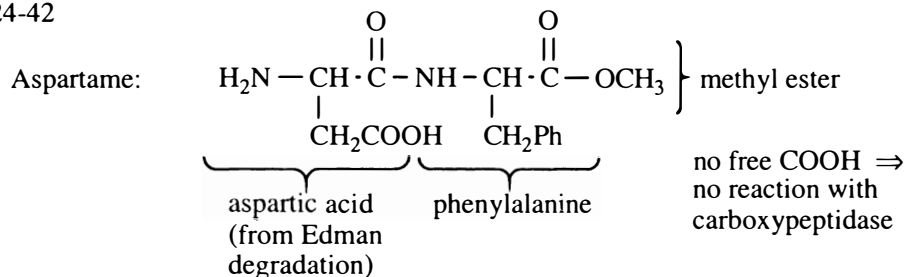


24-41



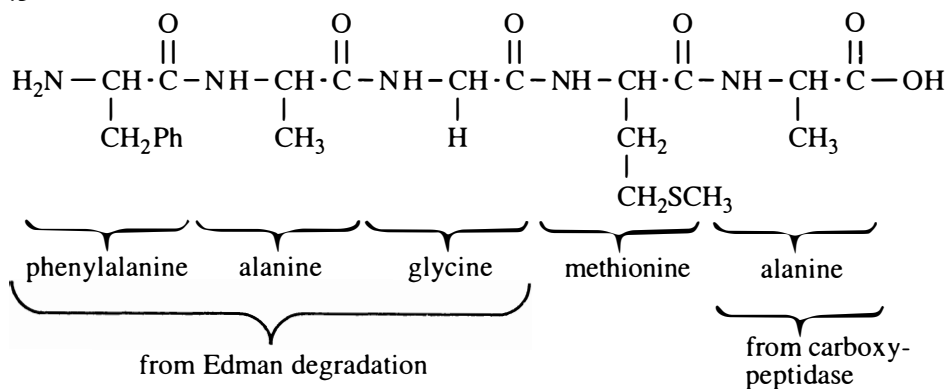
(d) glycylglutamylisoleucinamide; Gly—Gln—Ile • NH₂

24-42



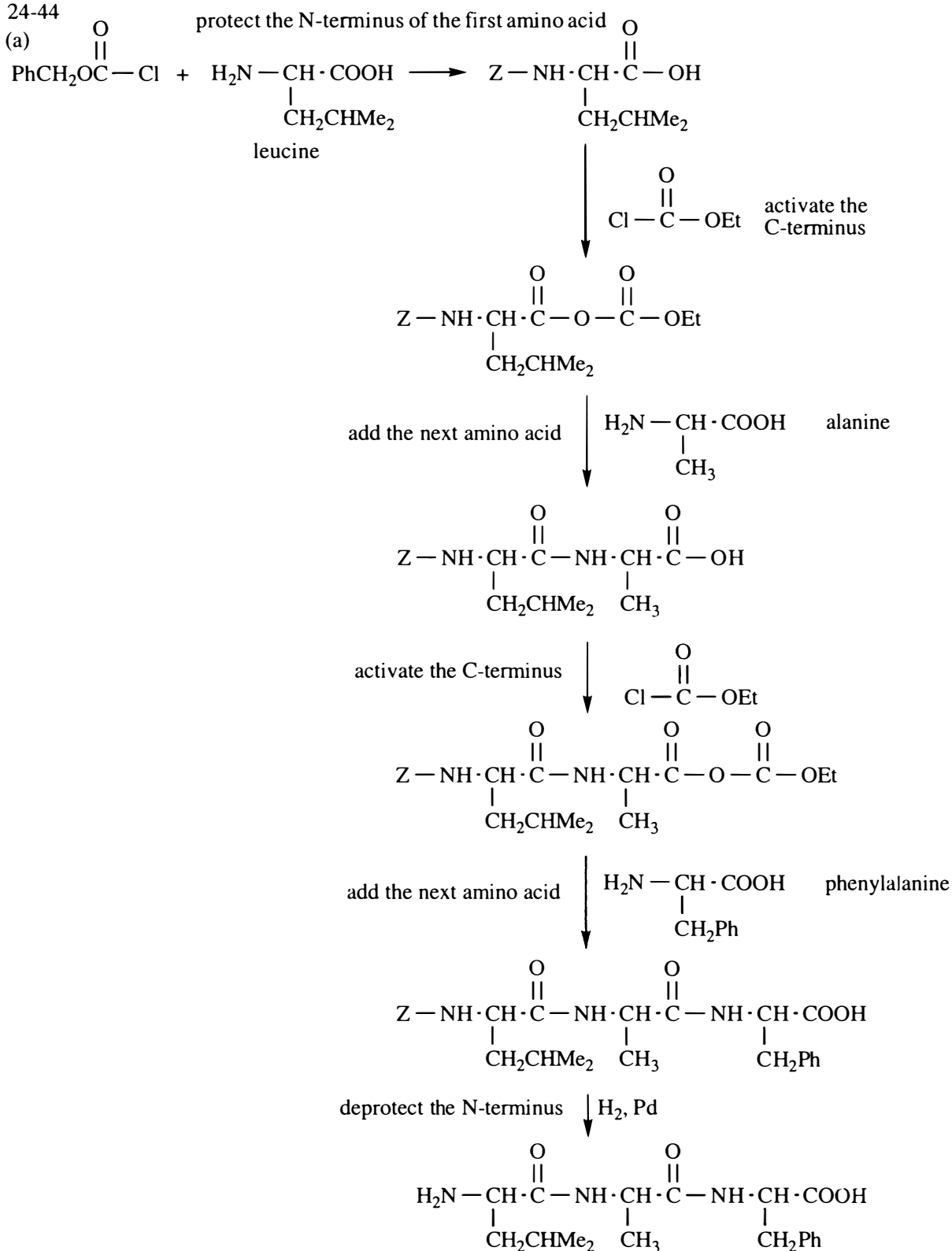
Aspartame is aspartylphenylalanine methyl ester.

24-43

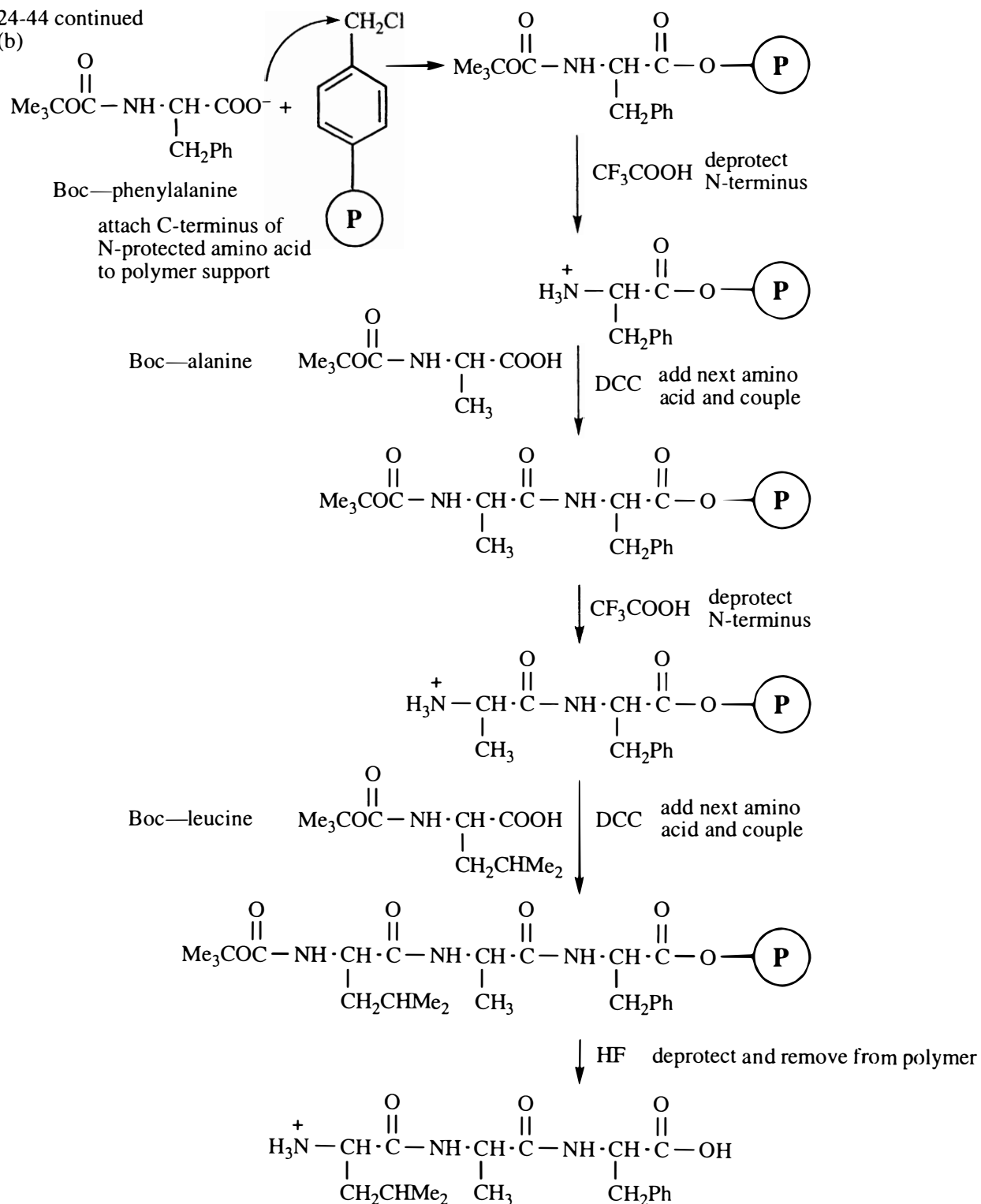


24-44

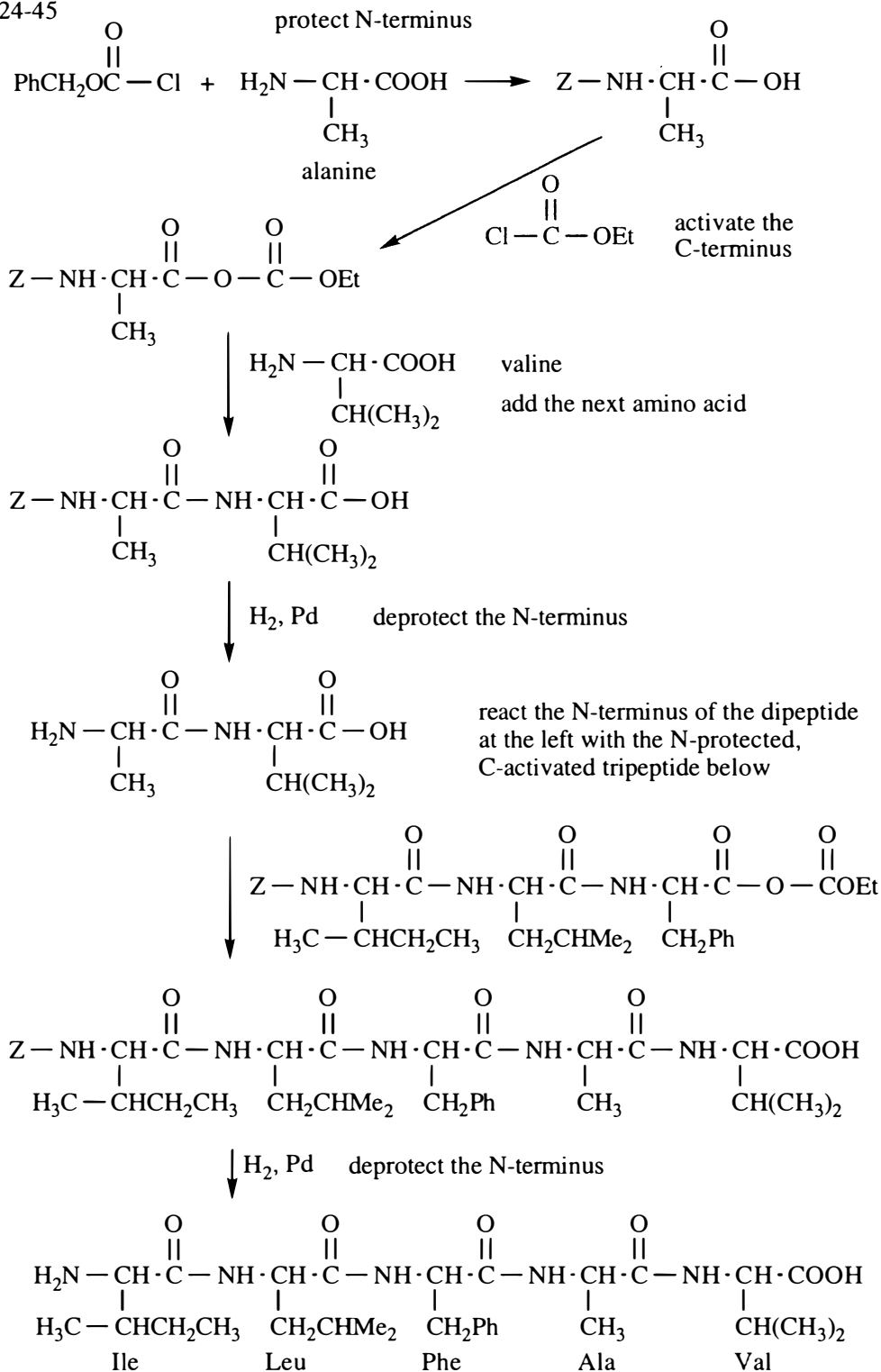
(a)



24-44 continued
(b)



24-45



24-46

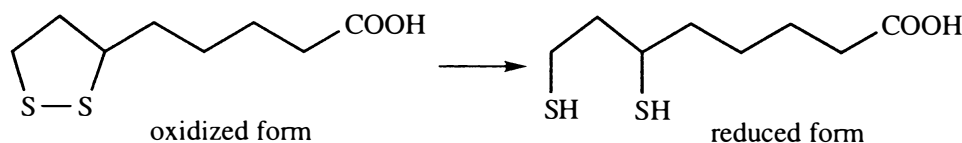
(a) There are two possible sources of ammonia in the hydrolysate. The C-terminus could have been present as the amide instead of the carboxyl, or the glutamic acid could have been present as its amide, glutamine.

(b) The C-terminus is present as the amide. The N-terminus is present as the lactam (cyclic amide) combining the amino group with the carboxyl group of the glutamic acid side chain.

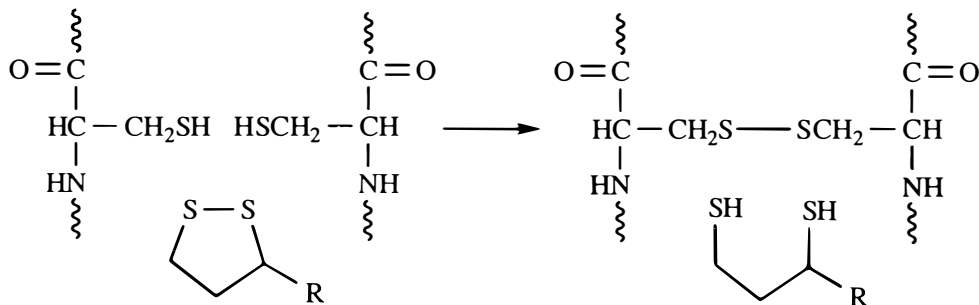
(c) The fact that hydrolysis does not release ammonia implies that the C-terminus is not an amide. Yet, carboxypeptidase treatment gives no reaction, showing that the C-terminus is not a free carboxyl group. Also, treatment with phenyl isothiocyanate gives no reaction, suggesting no free amine at the N-terminus. The most plausible explanation is that the N-terminus has reacted with the C-terminus to produce a cyclic amide, a lactam. (These large rings, called macrocycles, are often found in nature as hormones or antibiotics.)

24-47

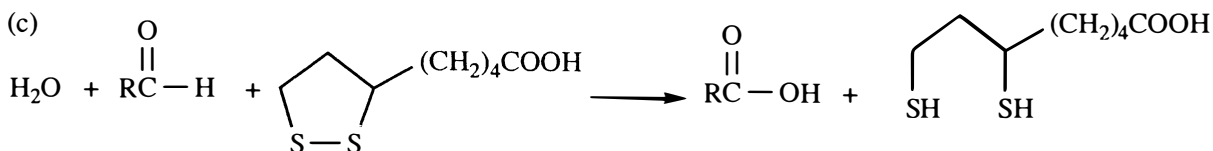
(a) Lipoic acid is a mild oxidizing agent. In the process of oxidizing another reactant, lipoic acid is reduced.



(b)

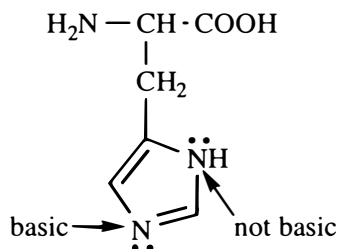


(c)

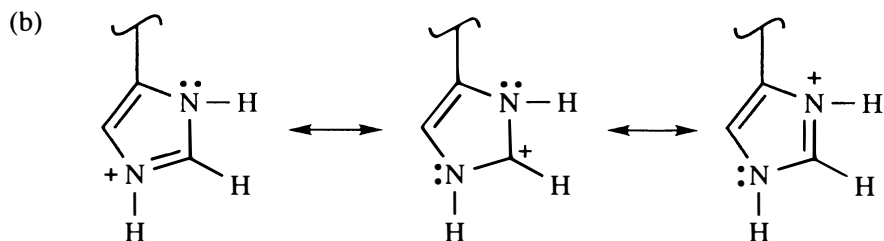


24-48

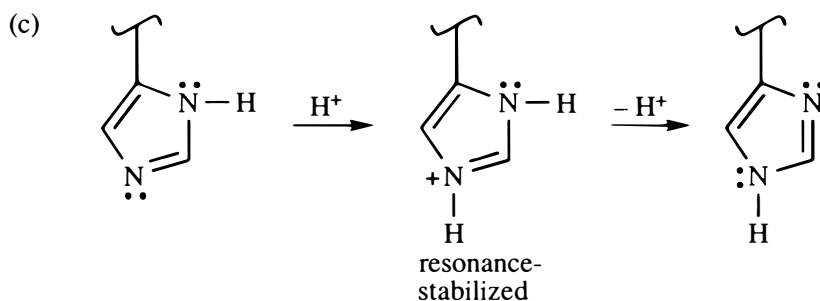
(a) histidine:



24-48 continued

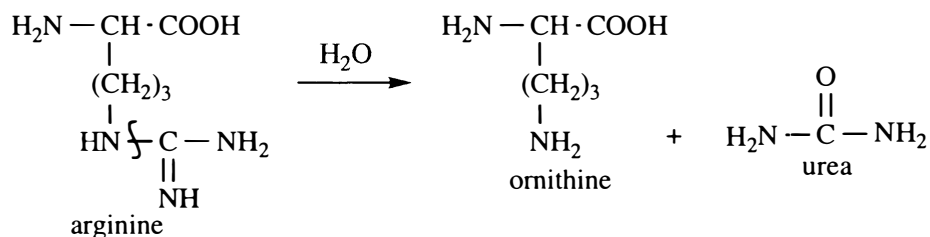


In the protonated imidazole, the two N's are similar in structure, and both NH groups are acidic.



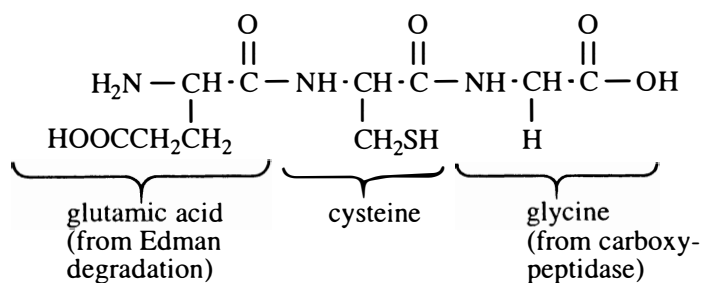
We usually think of protonation-deprotonation reactions occurring in solution where protons can move with solvent molecules. In an enzyme active-site, there is no "solvent", so there must be another mechanism for movement of protons. Often, conformational changes in the protein will move atoms closer or farther. Histidine serves the function of moving a proton toward or away from a particular site by using its different nitrogens in concert as a proton acceptor and a proton donor.

24-49 The high isoelectric point suggests a strongly basic side chain as in lysine. The N—CH₂ bond in the side chain of arginine is likely to have remained intact during the metabolism. (Can you propose a likely mechanism for this reaction?)



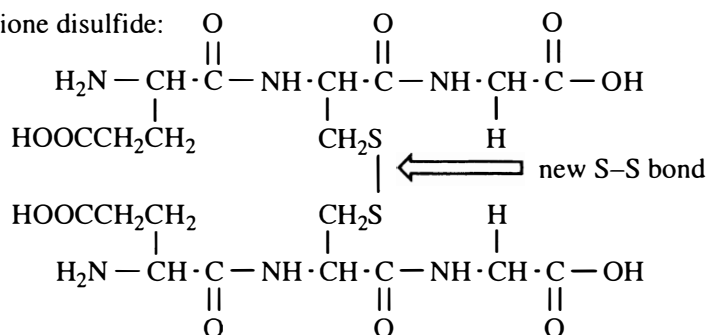
24-50

(a) glutathione:



(b) reaction: 2 glutathione + H₂O₂ → glutathione disulfide + 2 H₂O

structure of glutathione disulfide:



24-51

end groups: N-terminus Ala ————— Ile C-terminus

chymotrypsin fragments

A Glu—Gly—Tyr (middle)

B Ala—Lys—Phe

N-terminus

C Arg—(Ser? Leu?)—Ile

C-terminus

Ala—Lys—Phe—Glu Gly—Tyr—Arg—(Ser? Leu?)—Ile

trypsin fragments

D Ala—Lys

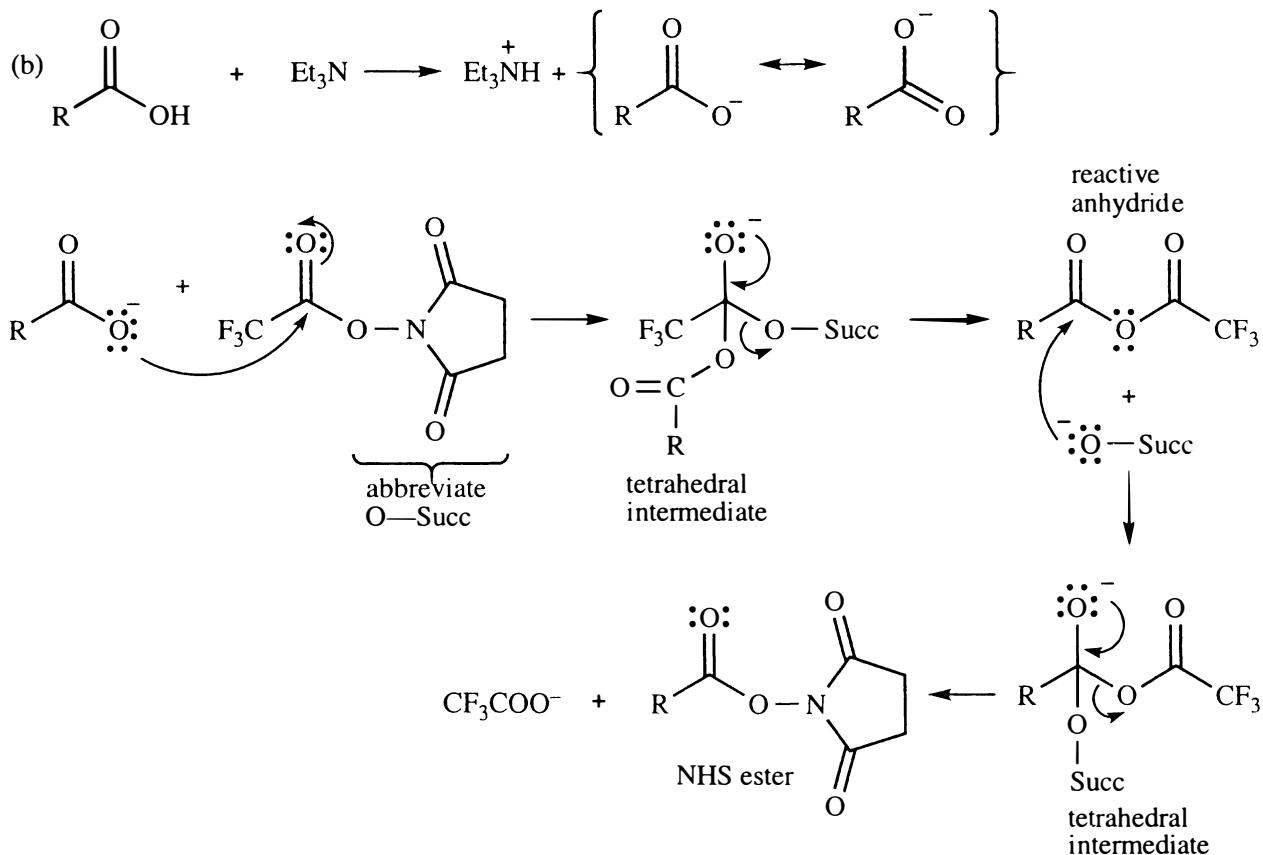
E Phe—Glu—Gly—Tyr—Arg

F Ser—Leu—Ile

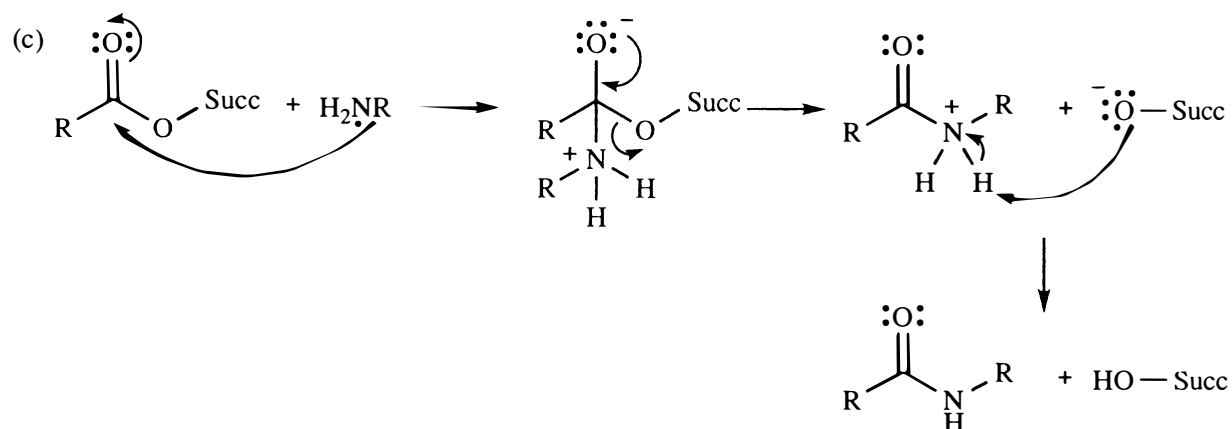
Ala—Lys—Phe—Glu—Gly—Tyr—Arg—Ser—Leu—Ile

24-52

(a) One important factor in ester reactivity is the ability of the alkoxy group to leave, and the main factor in determining leaving group ability is the stabilization of the anion. An NHS ester is more reactive than an alkyl ester because the anion R_2NO^- has an electron-withdrawing group on the O^- , thereby distributing the negative charge over two atoms instead of just one. A simple alkyl ester has the full negative charge on the oxygen with nowhere to go, RO^- .

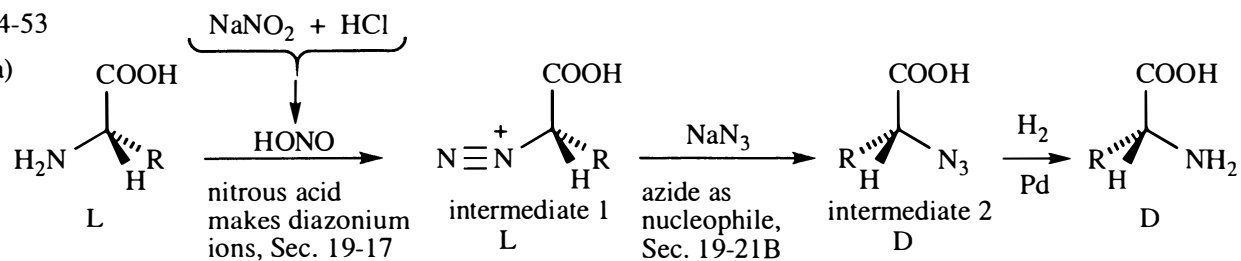


NHS trifluoroacetate is an amazing reagent. Not only does it activate the carboxylic acid through a mixed anhydride to form an ester under mild conditions, but the NHS leaving group is also the nucleophile that forms an ester that is both stable enough to work with, yet easily reactive when it needs to be. Perfect!



24-53

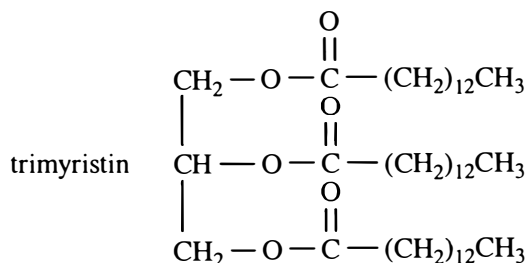
(a)



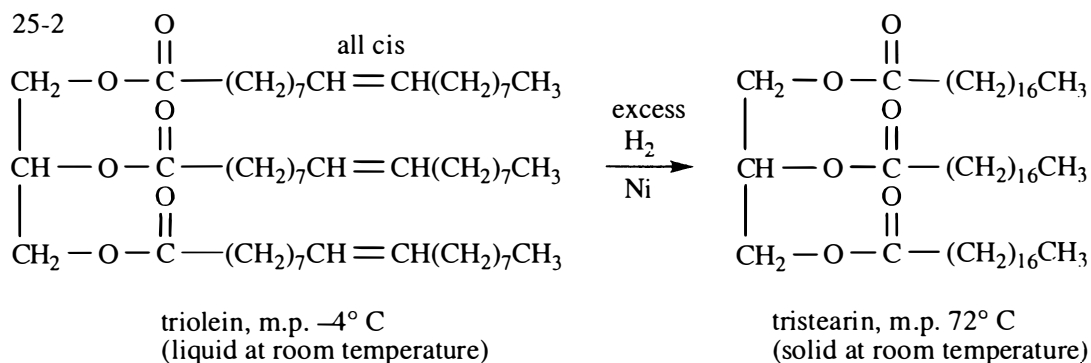
(b) The product has the opposite configuration from the starting because of the stereochemistry of the reactions. Diazotization does not break a bond to the chiral center so the L configuration is retained in Reaction 1. It is well documented that azide substitution is an $\text{S}_{\text{N}}2$ process that proceeds with inversion of configuration; this is why this process works. The third reaction does not break or form a bond to the chiral center, so the D configuration is retained.

CHAPTER 25—LIPIDS

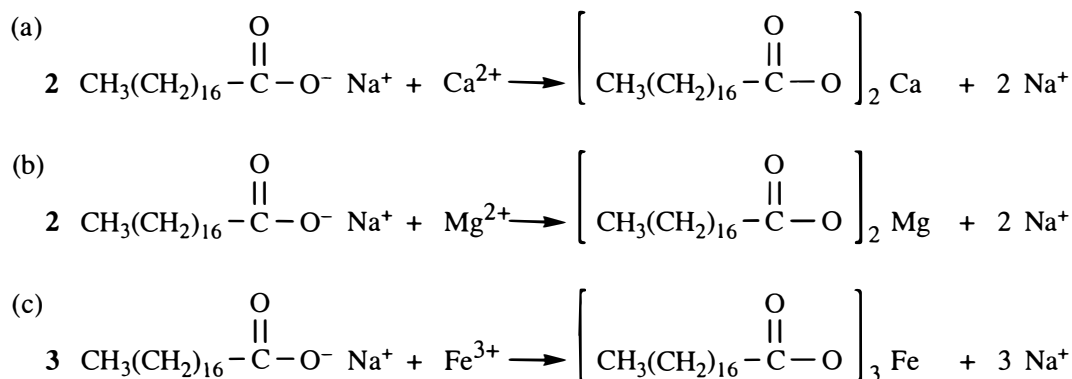
25-1



25-2



25-3



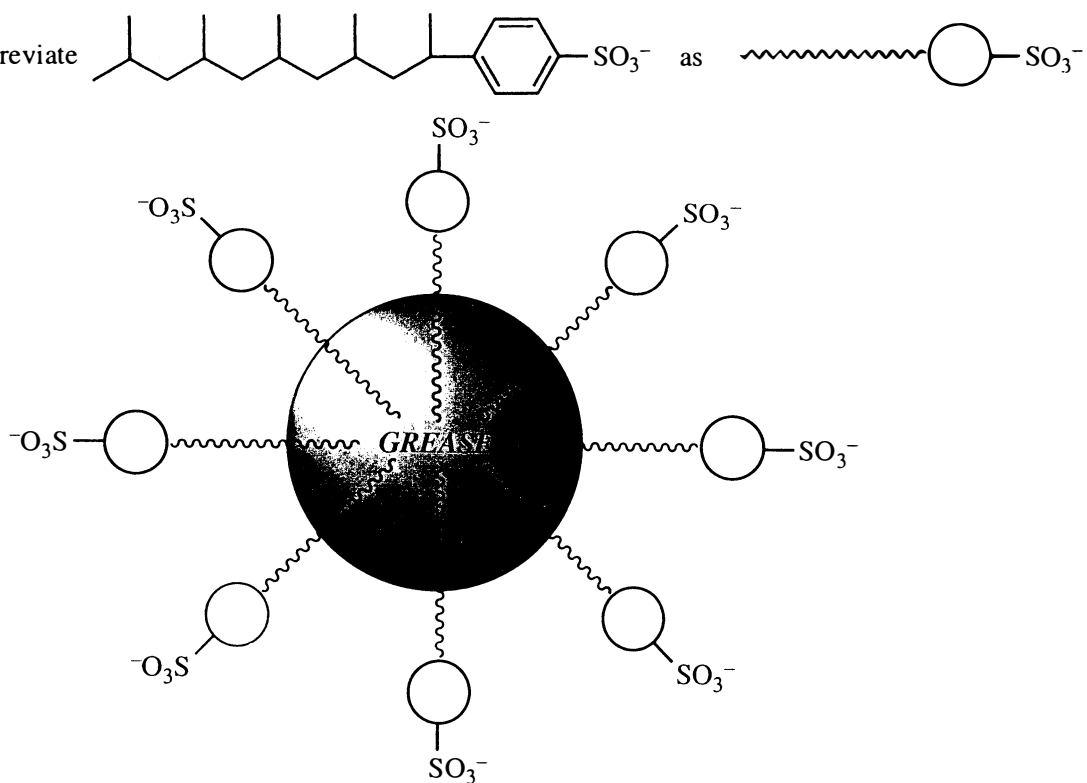
25-4

(a) Both sodium carbonate (its old name is "washing soda") and sodium phosphate will increase the pH above 6, so that the carboxyl group of the soap molecule will remain ionized, thus preventing precipitation.

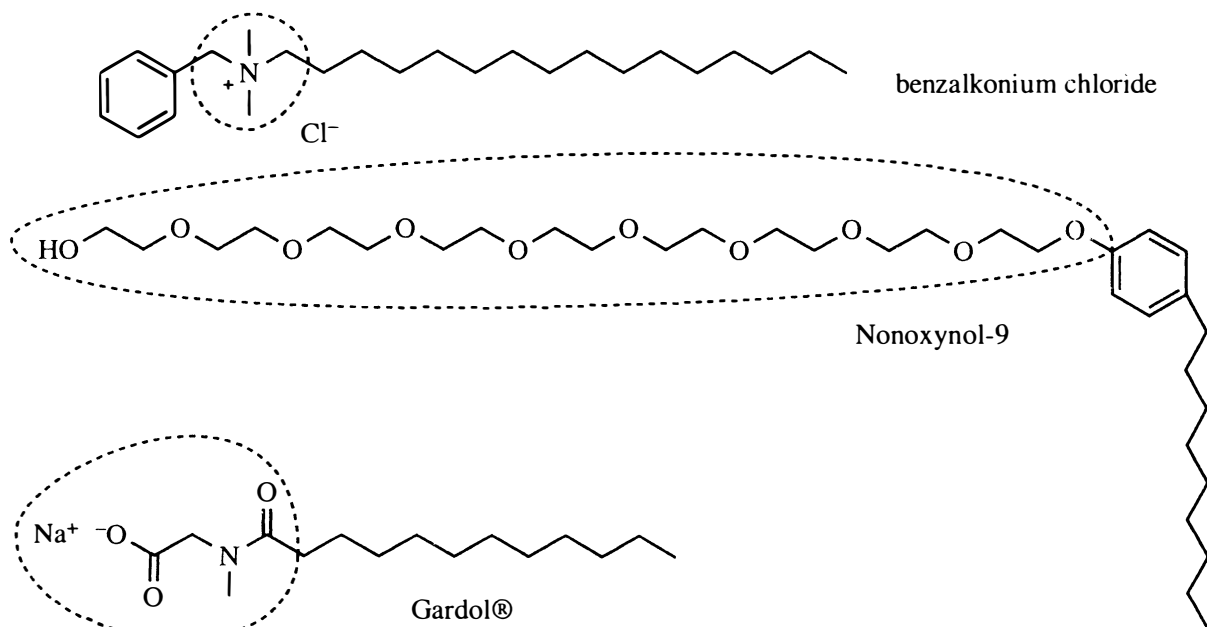
(b) In the presence of calcium, magnesium, and ferric ions, the carboxylate group of soap will form precipitates called "hard-water scum", or as scientists label it, "bathtub ring". Both carbonate and phosphate ions will form complexes or precipitates with these cations, thereby preventing precipitation of the soap from solution.

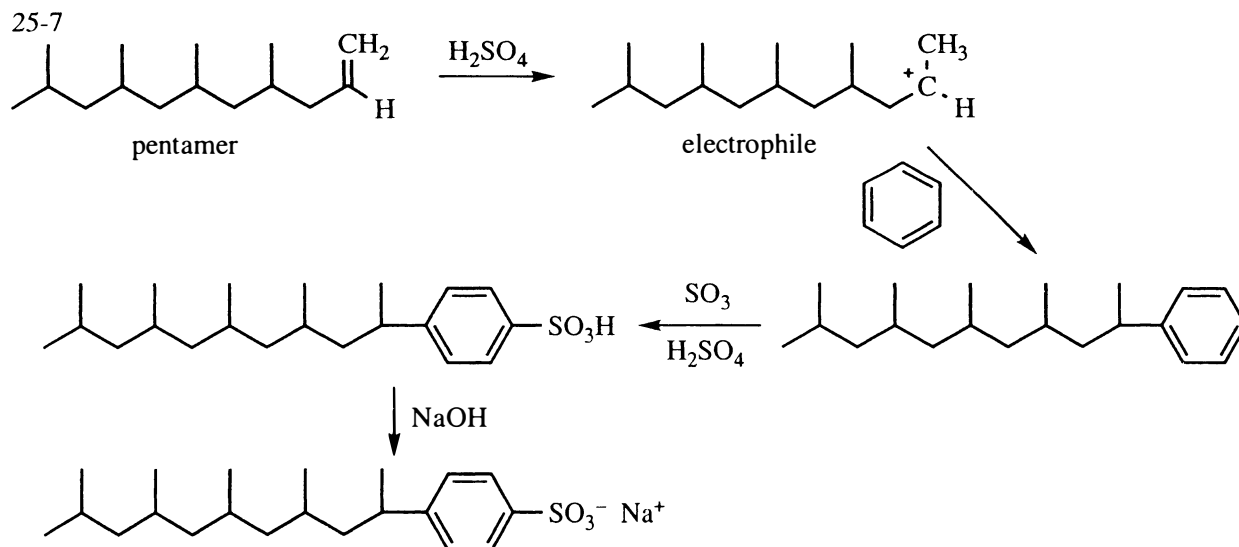
25-5

abbreviate

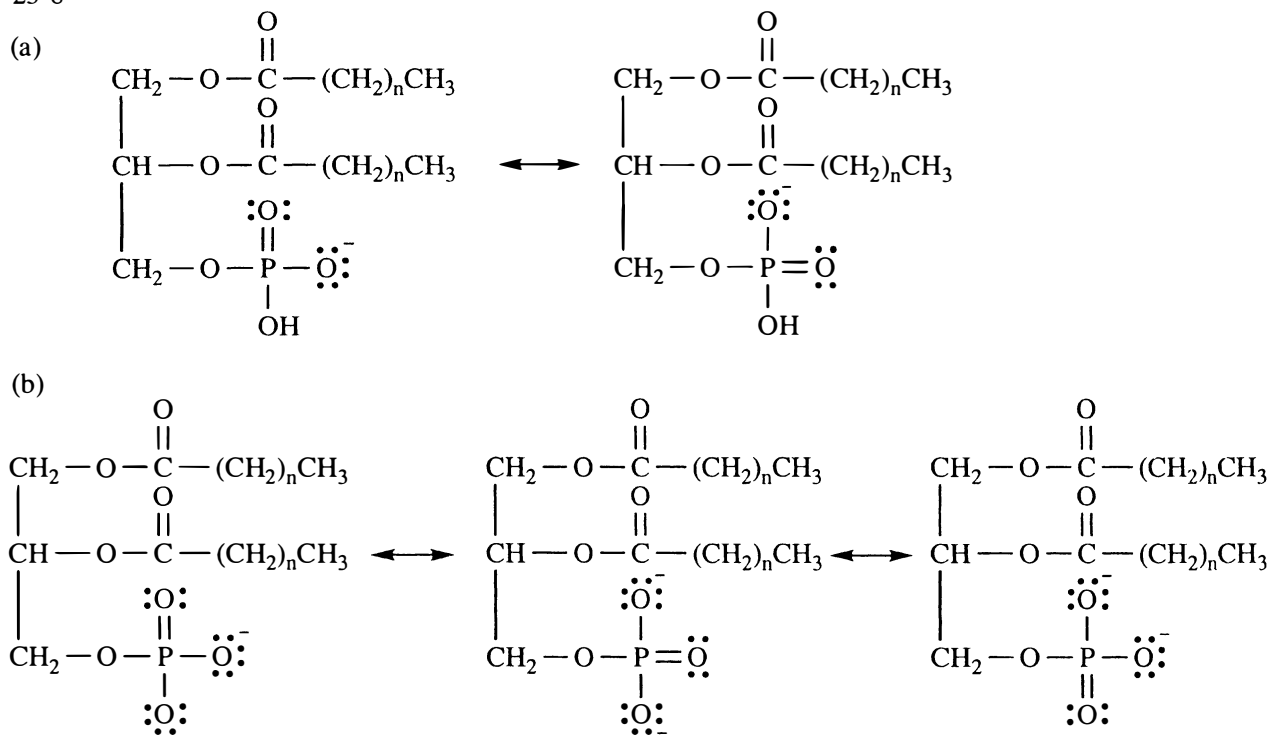


25-6 In each structure, the hydrophilic portion is circled. The uncircled part is hydrophobic.



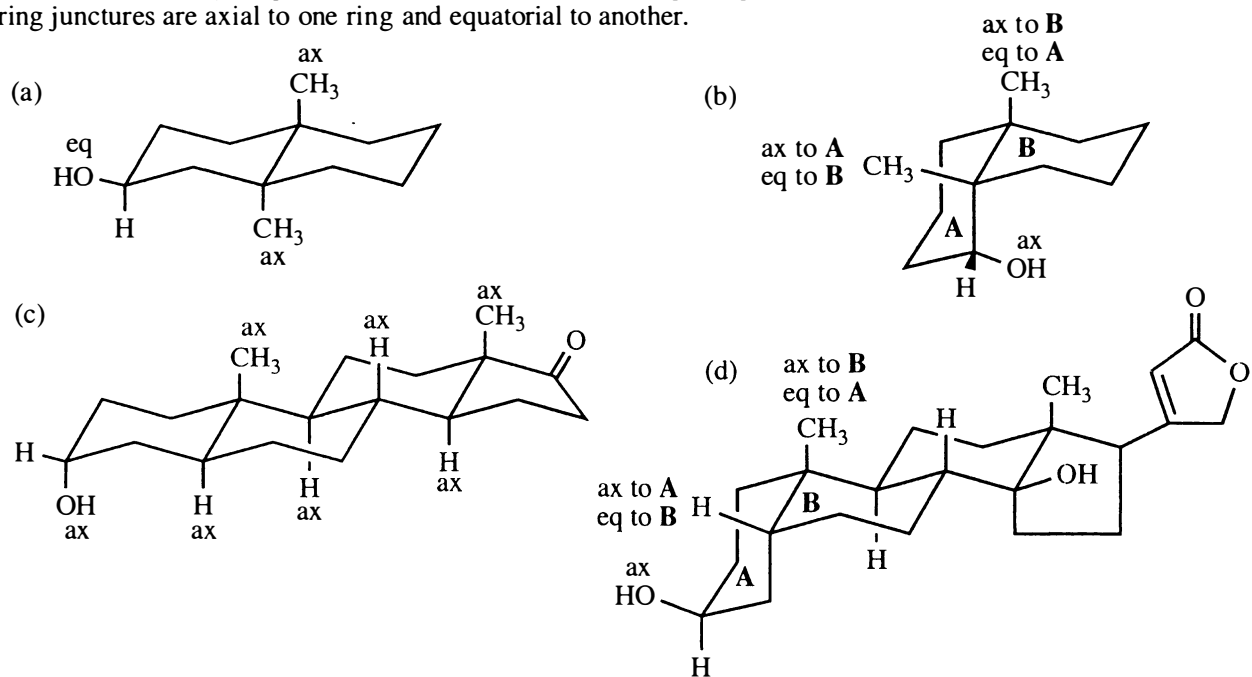


25-8

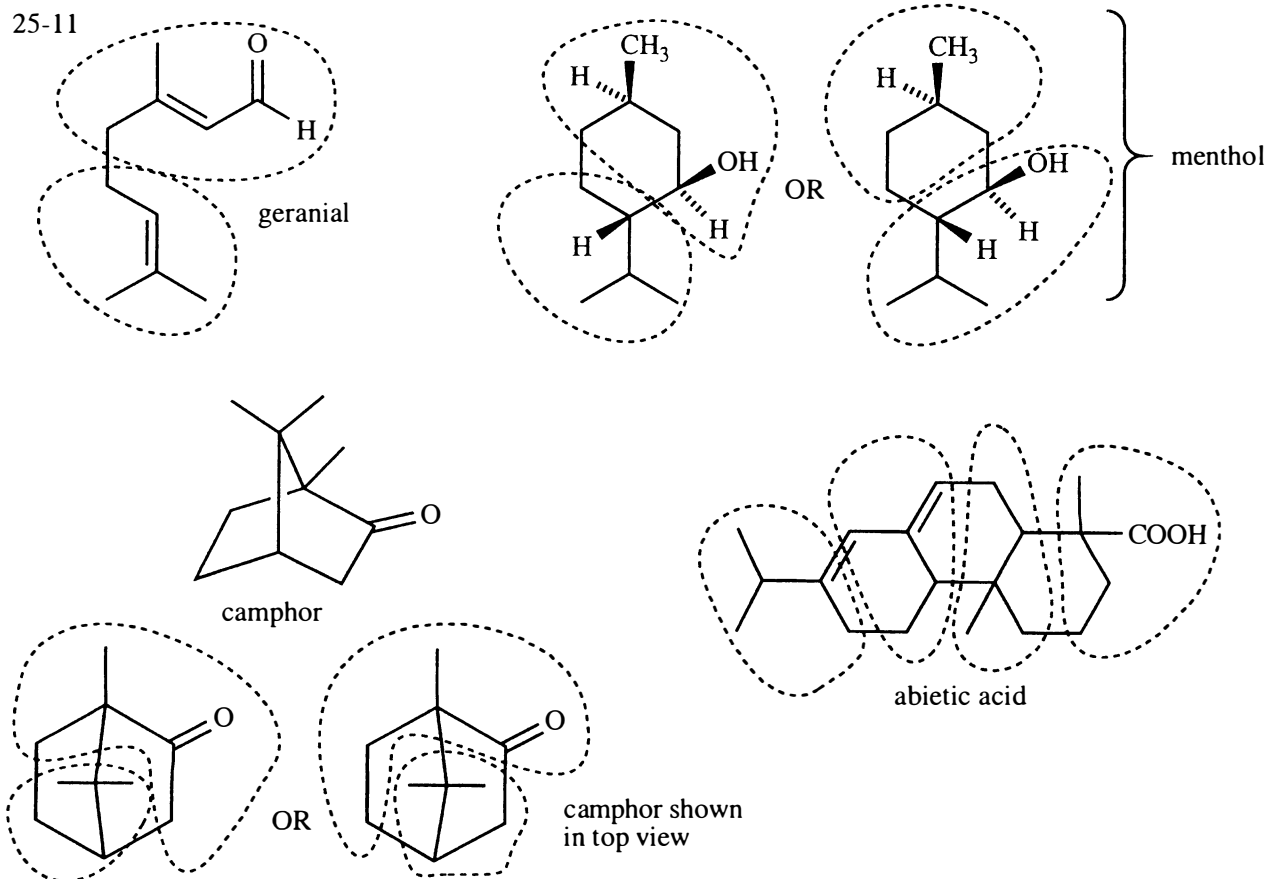


25-9 Estradiol is a phenol and can be ionized with aqueous NaOH. Testosterone does not have any hydrogens acidic enough to react with NaOH. Treatment of a solution of estradiol and testosterone in organic solvent with aqueous base will extract the phenoxide form of estradiol into the aqueous layer, leaving testosterone in the organic layer. Acidification of the aqueous base will precipitate estradiol which can be filtered. Evaporation of the organic solvent will leave testosterone.

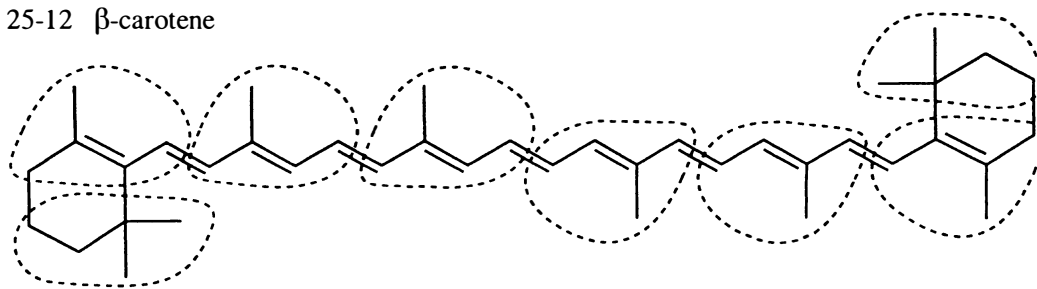
25-10 Models may help. Abbreviations: "ax" = axial; "eq" = equatorial. Note that substituents at *cis*-fused ring junctures are axial to one ring and equatorial to another.



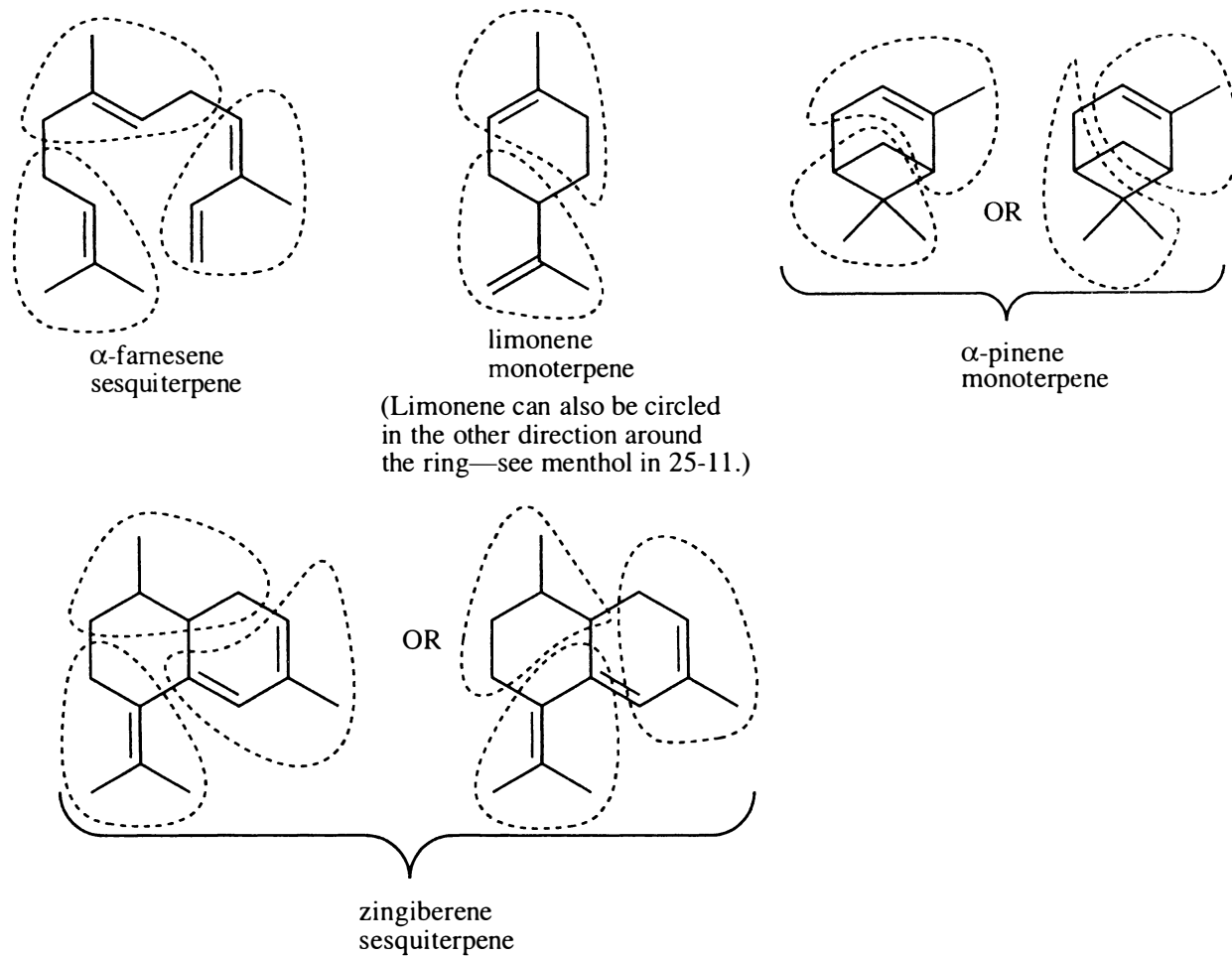
25-11



25-12 β -carotene



25-13

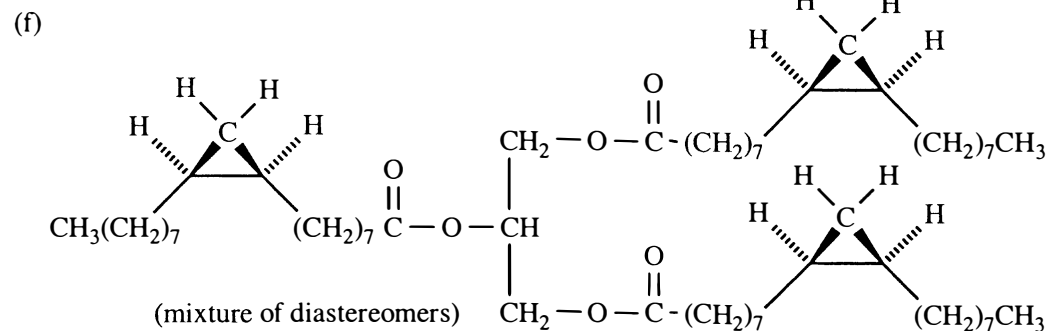
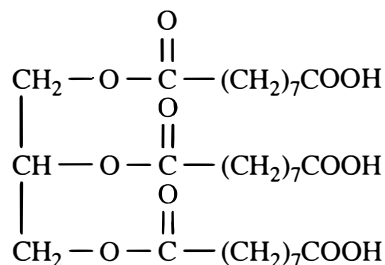
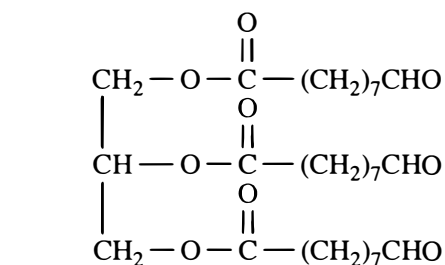
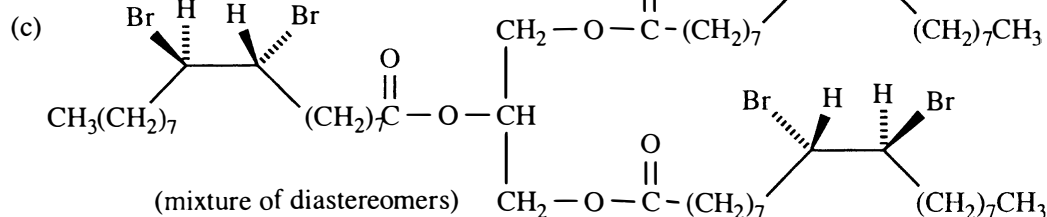


25-14 Please refer to problem 1-20, page 12 of this Solutions Manual.

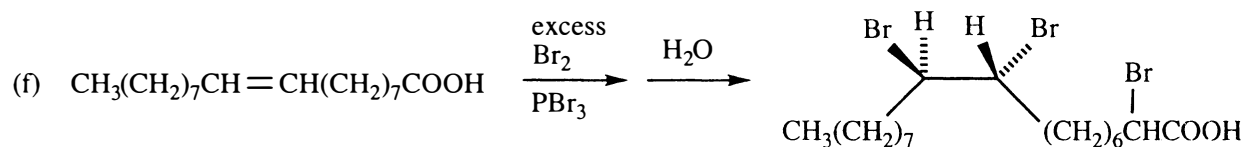
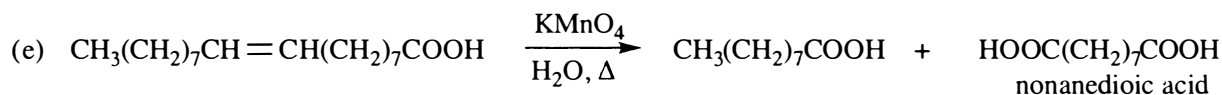
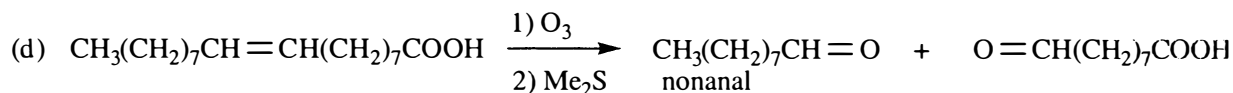
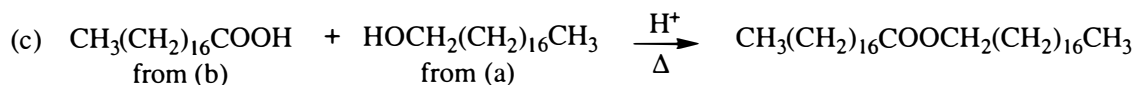
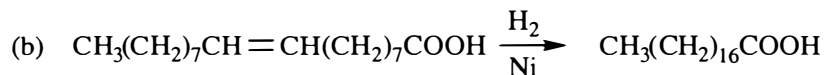
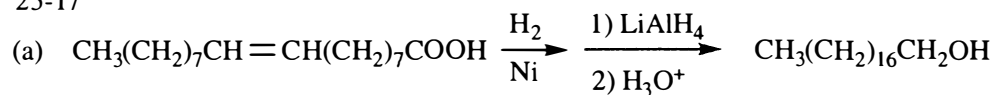
25-15

- (a) triglyceride (b) synthetic detergent (c) wax (d) sesquiterpene (e) steroid

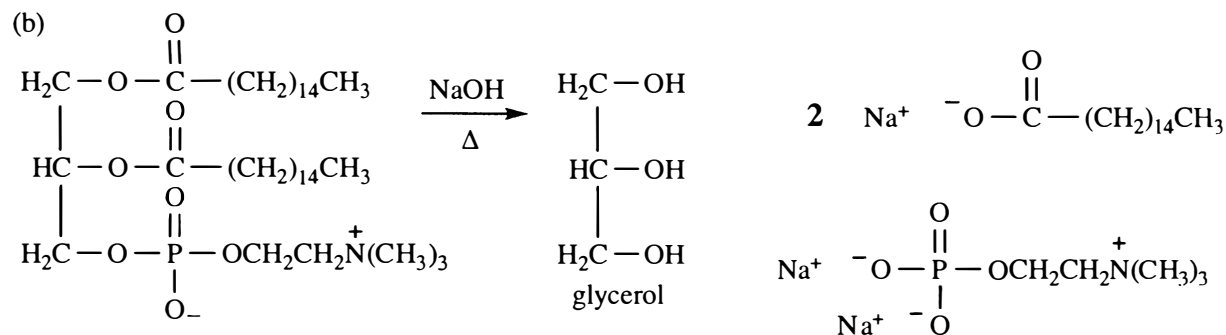
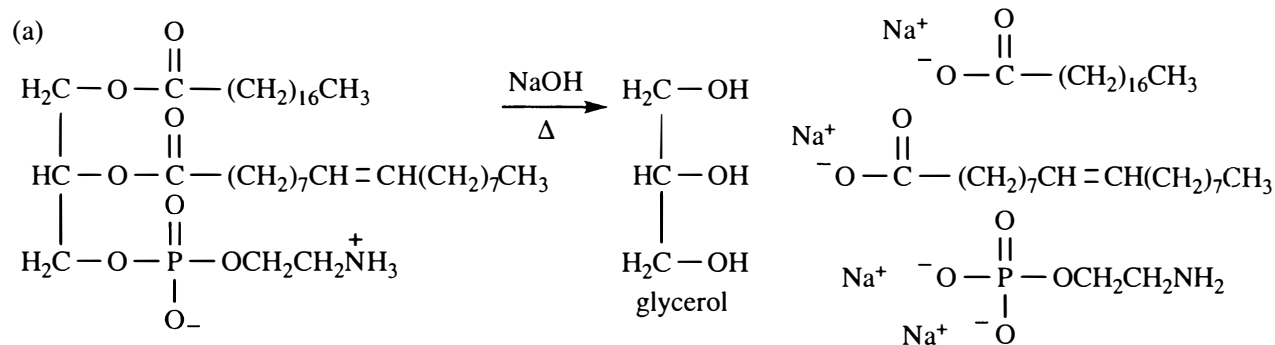
(a) $3 \text{ CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COO}^- \text{Na}^+ + \text{HOCH}(\text{CH}_2\text{OH})_2$
 soap glycerol

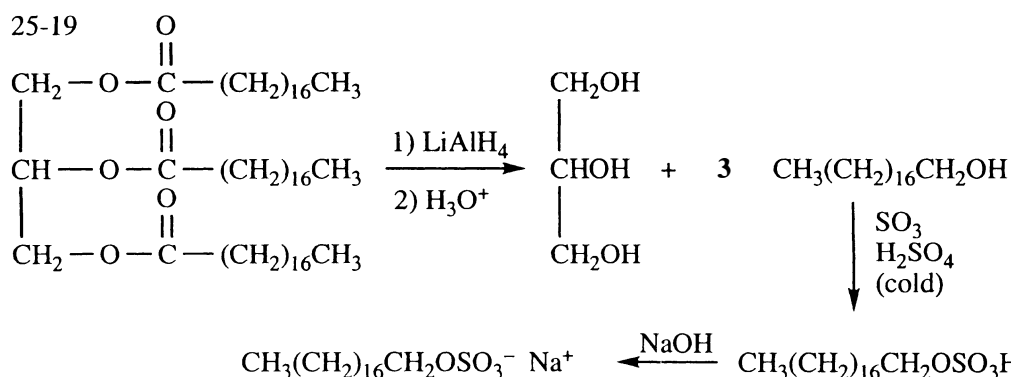


25-17



25-18





25-20 Reagents in parts (a), (b), and (d) would react with alkenes. If both samples contained alkenes, these reagents could not distinguish the samples. Saponification (part (c)), however, is a reaction of an ester, so only the vegetable oil would react, not the hydrocarbon oil mixture.

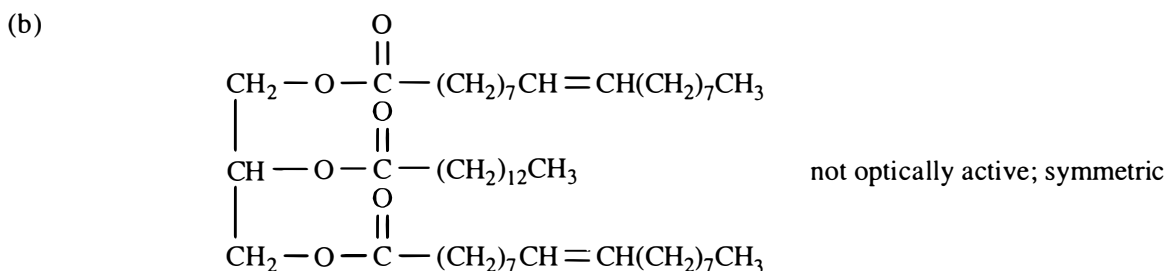
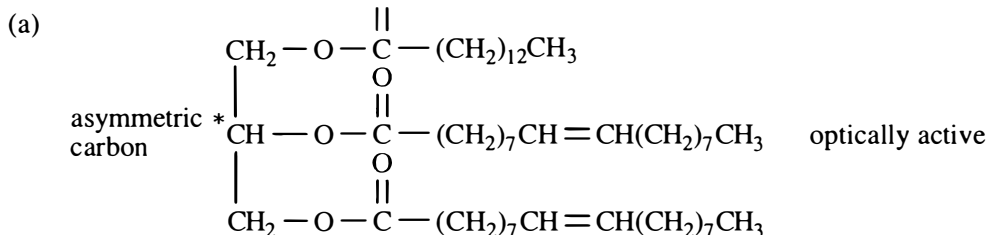
25-21 (a) Add an aqueous solution of calcium ion or magnesium ion. Sodium stearate will produce a precipitate, while the sulfonate will not precipitate.

(b) Beeswax, an ester, can be saponified with NaOH. Paraffin wax is a solid mixture of alkanes and will not react.

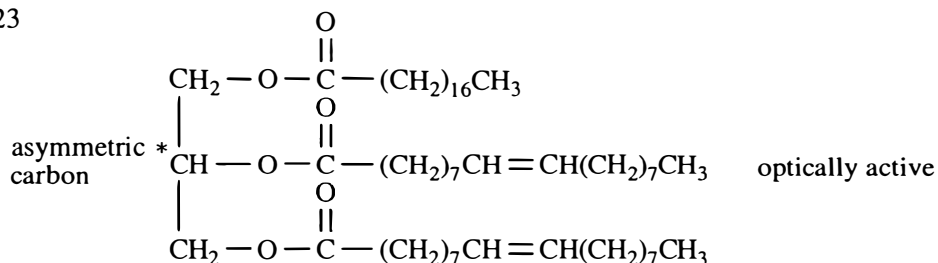
(c) Myristic acid will dissolve (or be emulsified) in dilute aqueous base. Trimyristin will remain unaffected.

(d) Triolein (an unsaturated oil) will decolorize bromine in CCl_4 , but trimyristin (a saturated fat) will not.

25-22

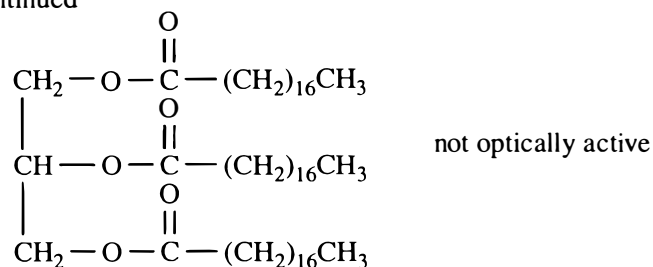


25-23

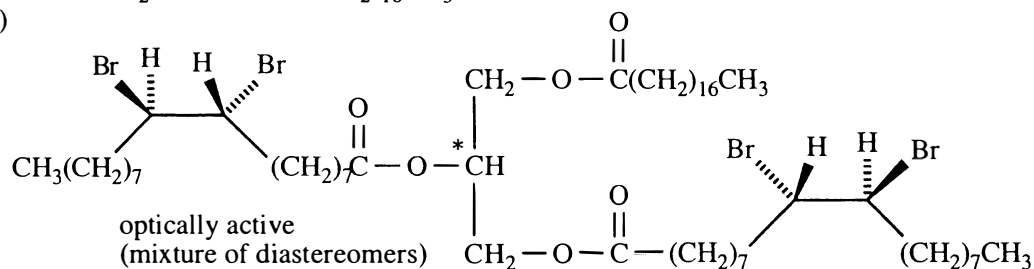


25-23 continued

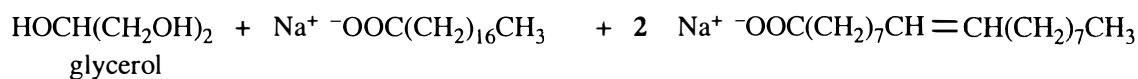
(a)



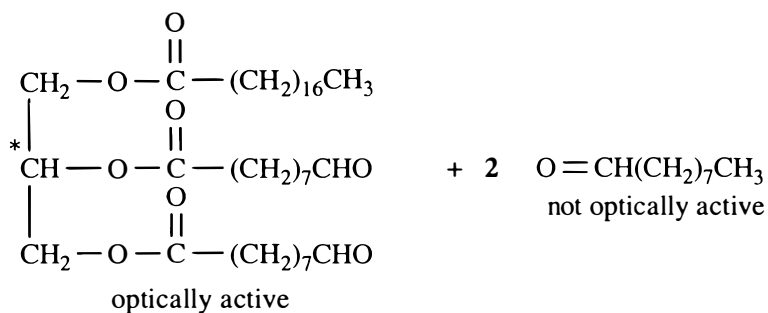
(b)



(c) products are not optically active

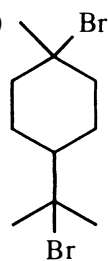


(d)

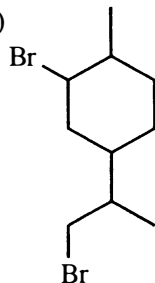


25-24 The products in (b), (c) and (f) are mixtures of stereoisomers.

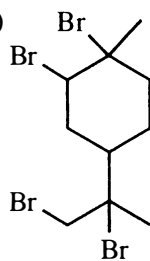
(a)



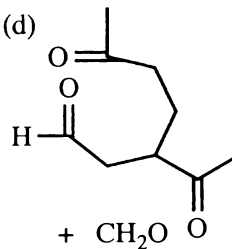
(b)



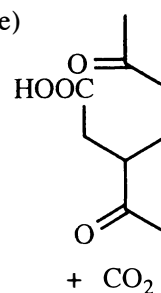
(c)



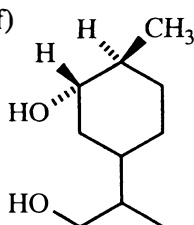
(d)



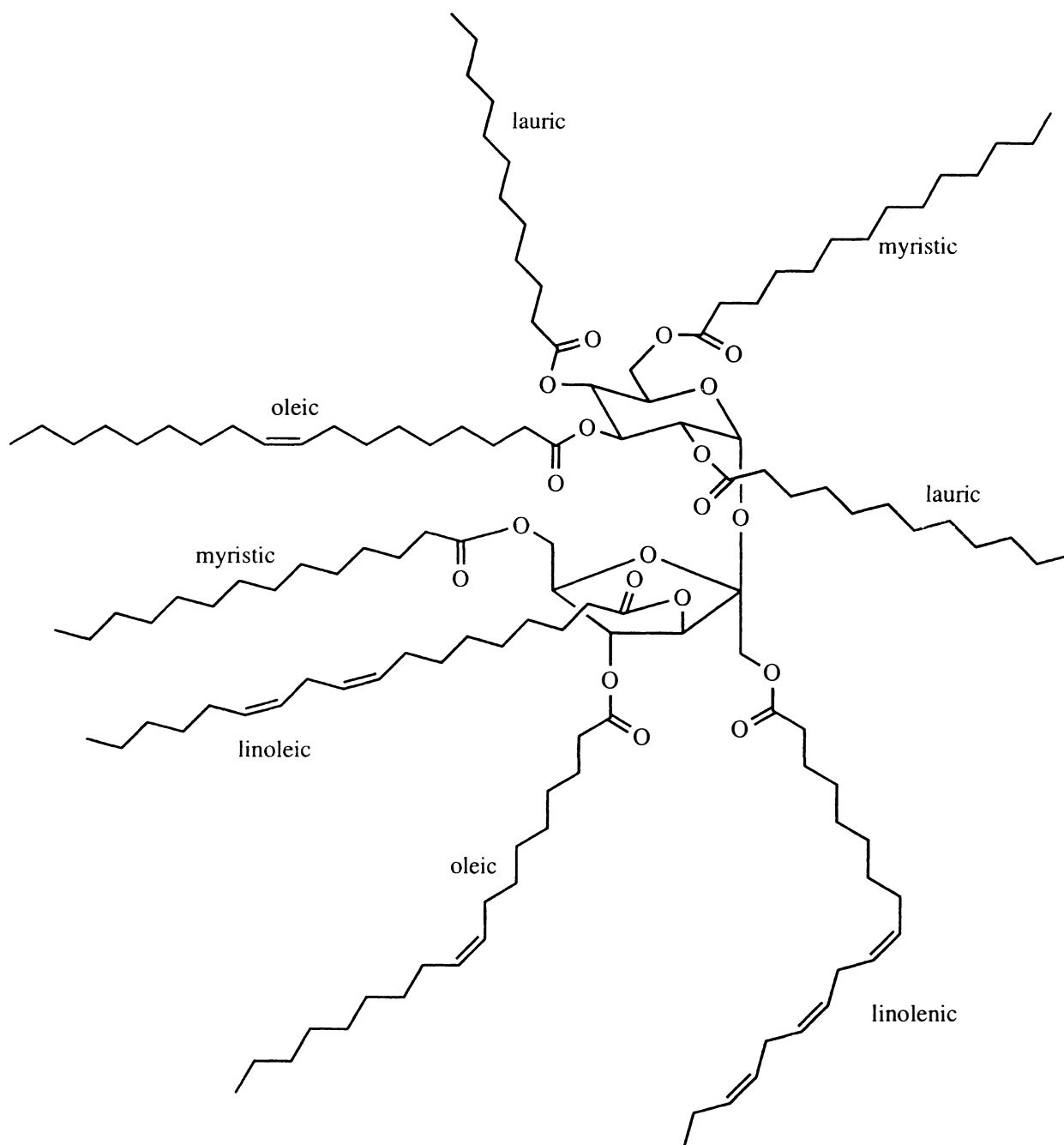
(e)



(f)

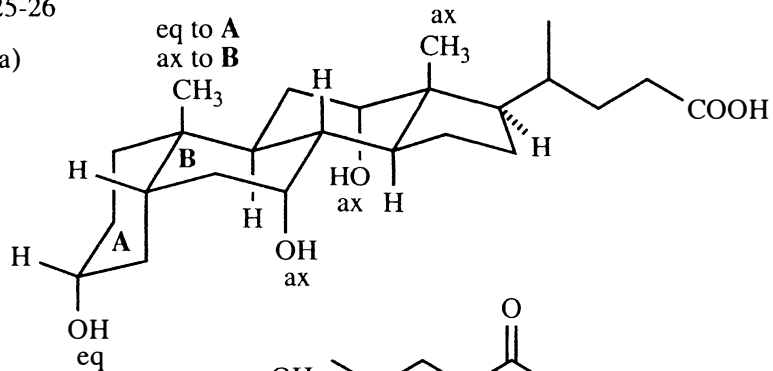


25-25 Is it any wonder that Olestra cannot be digested!

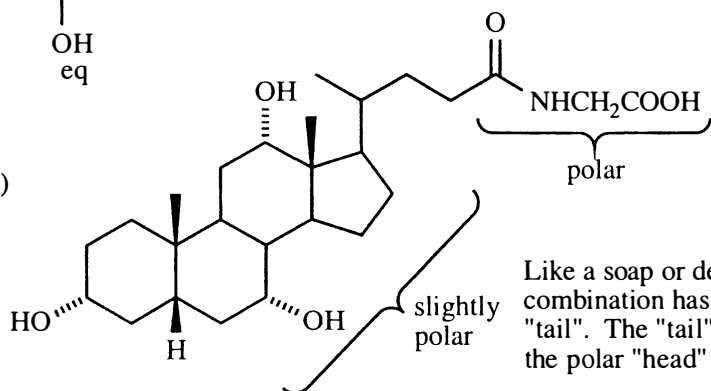


25-26

(a)



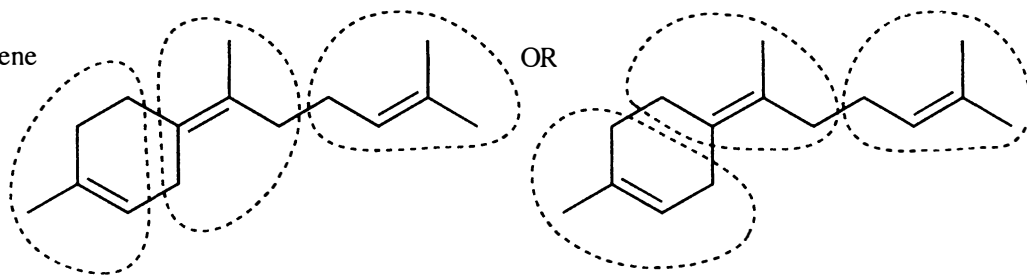
(b)



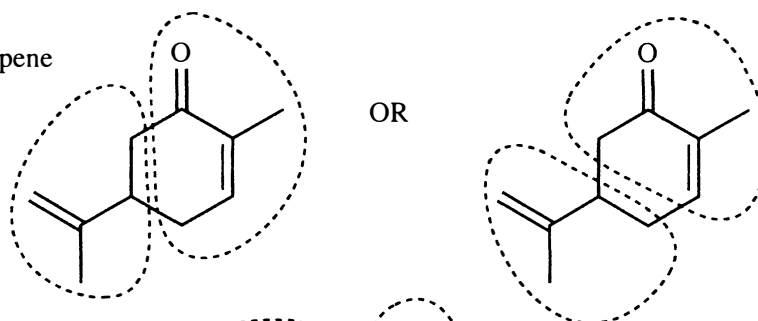
Like a soap or detergent, this cholic acid—glycine combination has a very polar "head" and a slightly polar "tail". The "tail" can dissolve non-polar molecules and the polar "head" can carry the complex into polar media.

25-27

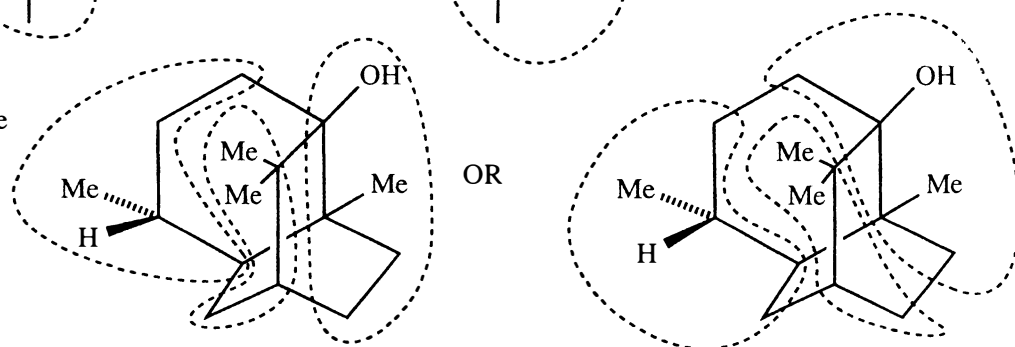
(a) sesquiterpene



(b) monoterpene

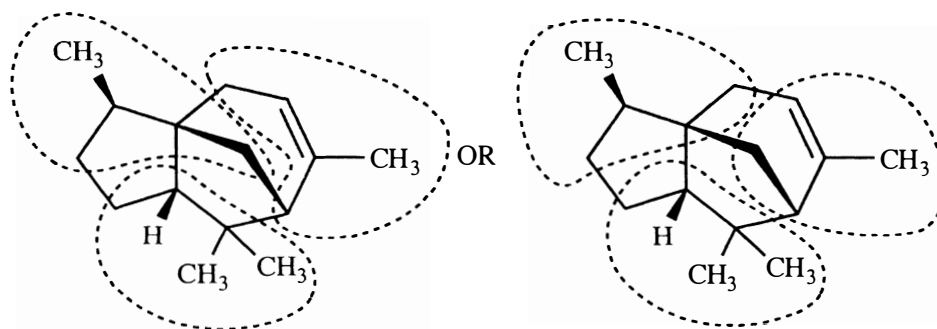


(c) sesquiterpene

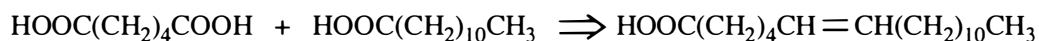


25-27

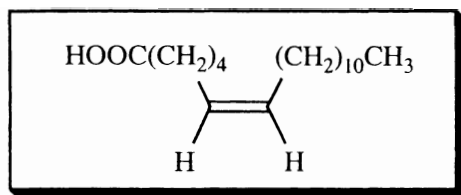
(d) sesquiterpene



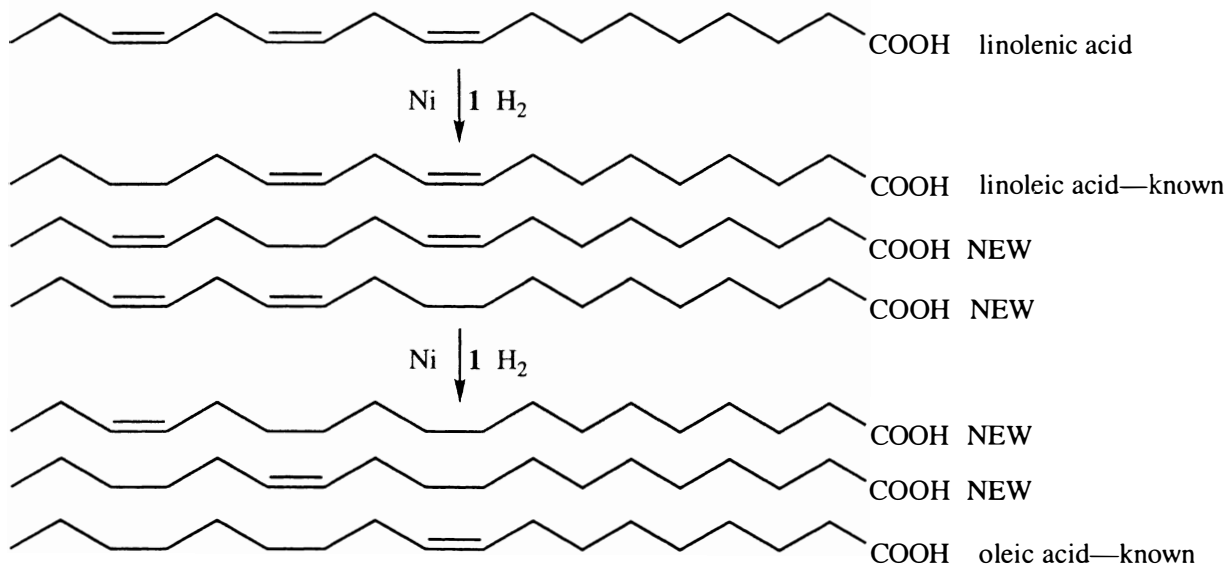
25-28 The formula $C_{18}H_{34}O_2$ has two elements of unsaturation; one is the carbonyl, so the other must be an alkene or a ring. Catalytic hydrogenation gives stearic acid, so the carbon cannot include a ring; it must contain an alkene. The products from $KMnO_4$ oxidation determine the location of the alkene:



If the alkene were *trans*, the coupling constant for the vinyl protons would be about 15 Hz; a 10 Hz coupling constant indicates a *cis* alkene. The 7 Hz coupling is from the vinyl H's to the neighboring CH_2 's.



25-29



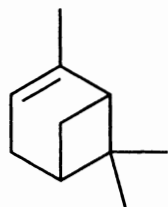
In addition to the new isomers with different positions of the double bonds, there has been growing concern over the *trans* fatty acids created by isomerizing the naturally occurring *cis* double bonds. More manufacturers are now listing the percent of "*trans* fat" on their food labels.

25-30 The cetyl glycoside would be a good emulsifying agent. It has a polar end (glucose) and a non-polar end (the hydrocarbon chain), so it can dissolve non-polar molecules, then carry them through polar media in micelles. This is found in Nature where non-polar molecules such as steroid hormones, antibiotics, and other physiologically-active compounds are carried through the bloodstream (aqueous) by attaching saccharides (usually mono, di, or tri), making the non-polar group water soluble.

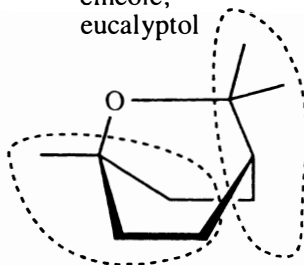
25-31 (a) Four of these components in Vicks Vapo-Rub® are terpenes. The only one that is not is decane; it is not comprised of isoprene units despite having the correct number of carbons for a monoterpene.

Three of the four terpenes have had their isoprene units indicated in previous problems; in each of those three, there are two possible ways to assign the isoprene units, so those pictures will not be duplicated here.

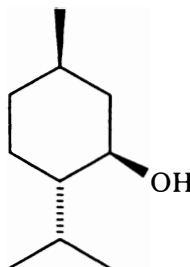
α -pinene;
see 25-13



cineole;
eucalyptol



menthol;
see 25-11



camphor;
see 25-11



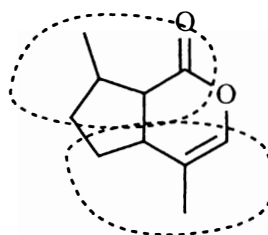
camphor



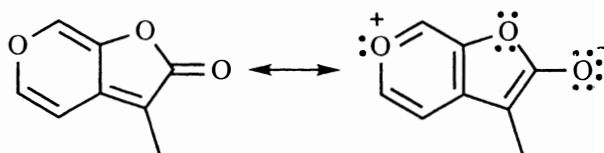
(b) Vicks Vapo-Rub® must be optically active as it contains four optically active terpenes.

25-32

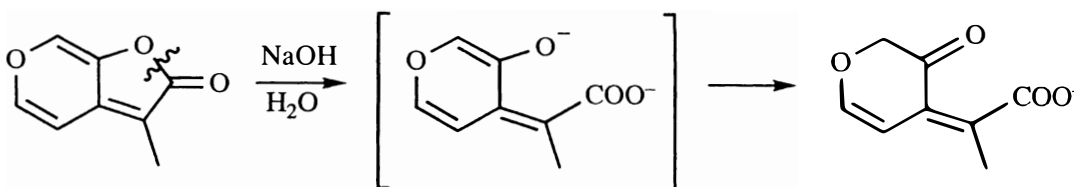
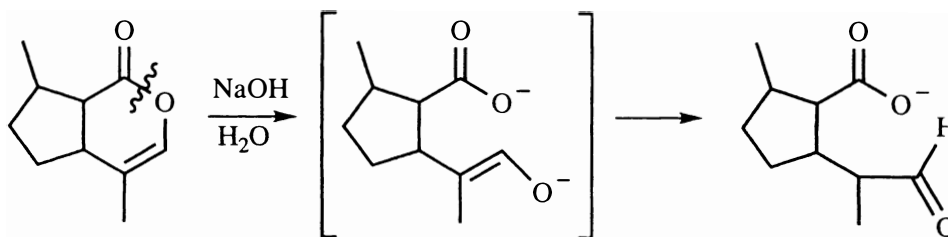
(a) Of the two, only nepetalactone is a terpene. The other has only 8 carbons and terpenes must be in multiples of 5 carbons.



(b) Of the two, only the second is aromatic as can be readily seen in one of the resonance forms.



(c) Each compound is cleaved with NaOH (aq) to give an enolate that tautomerizes to the more stable keto form.

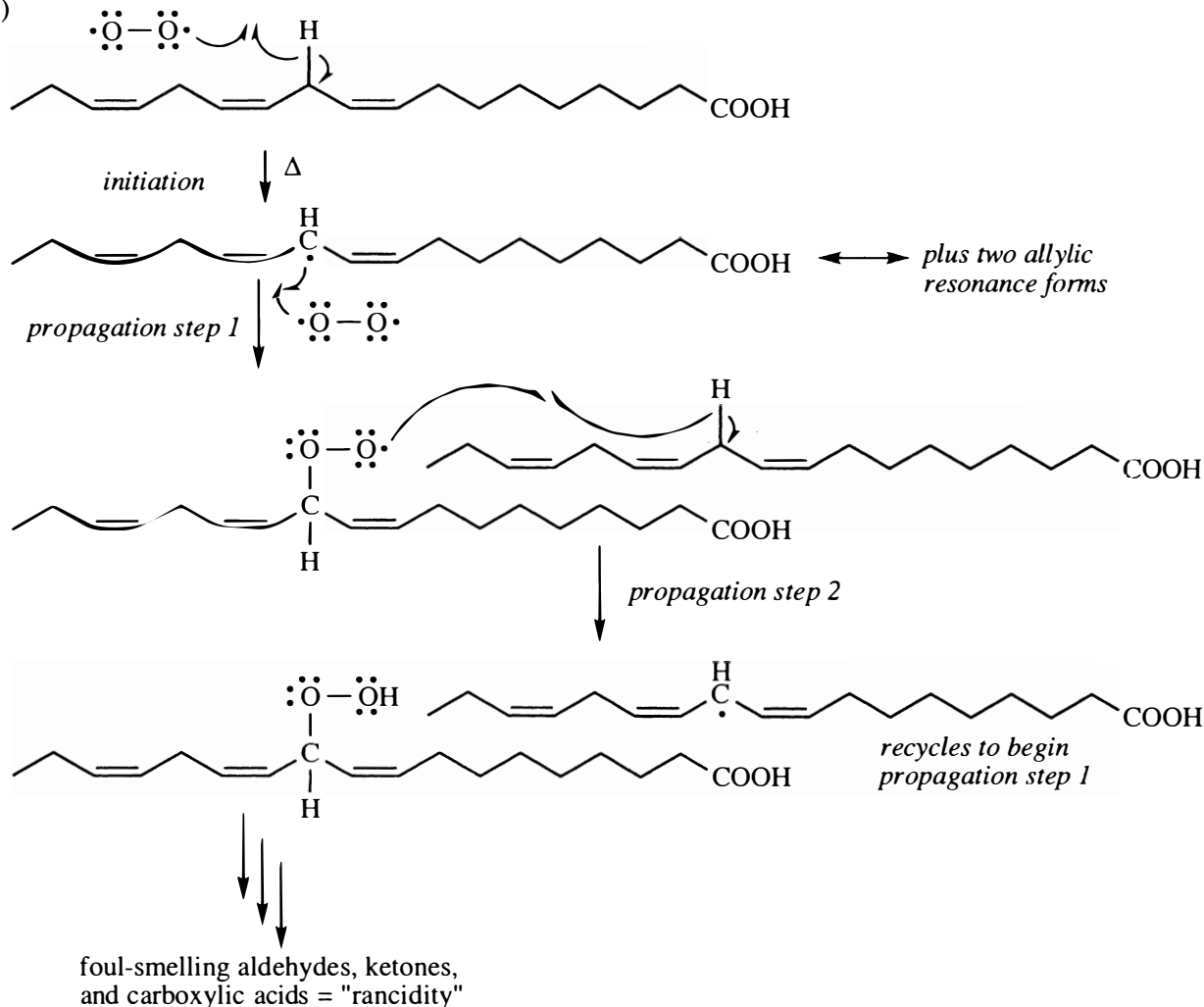


25-33

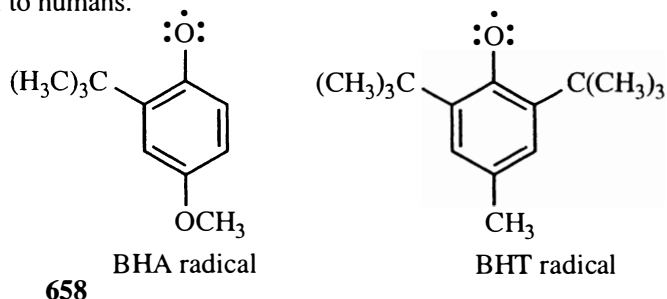
(a) High temperature and the diradical O_2 molecule strongly suggest a radical mechanism.

(b) Radical stability follows the order: benzylic > allylic > $3^\circ > 2^\circ > 1^\circ$. A radical at C-11 would be *doubly allylic* making it a prime site for radical reaction.

(c)



(d) Antioxidants are molecules that stop the free radical chain mechanism. In each of the two cases here, abstraction of the phenolic H makes an oxygen radical that is highly stabilized by resonance, so stable that it does not continue the free radical chain process. It only takes a small amount of antioxidant to prevent the chain mechanism. Interestingly, in breakfast cereals, the antioxidant is usually put in the plastic bag that the cereal is packaged in, rather than in the food itself. BHA and BHT can also be used directly in food as there is no evidence that they are harmful to humans.

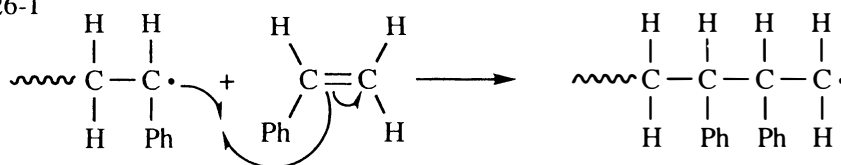


CHAPTER 26—SYNTHETIC POLYMERS

Note: In this chapter, the "wavy bond" symbol means the continuation of a polymer chain.



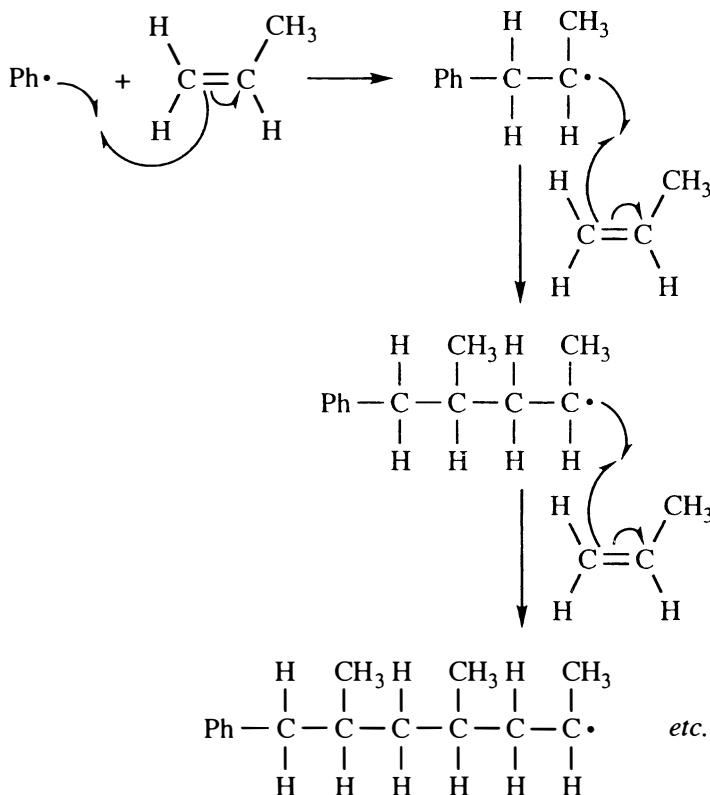
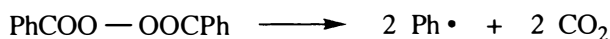
26-1



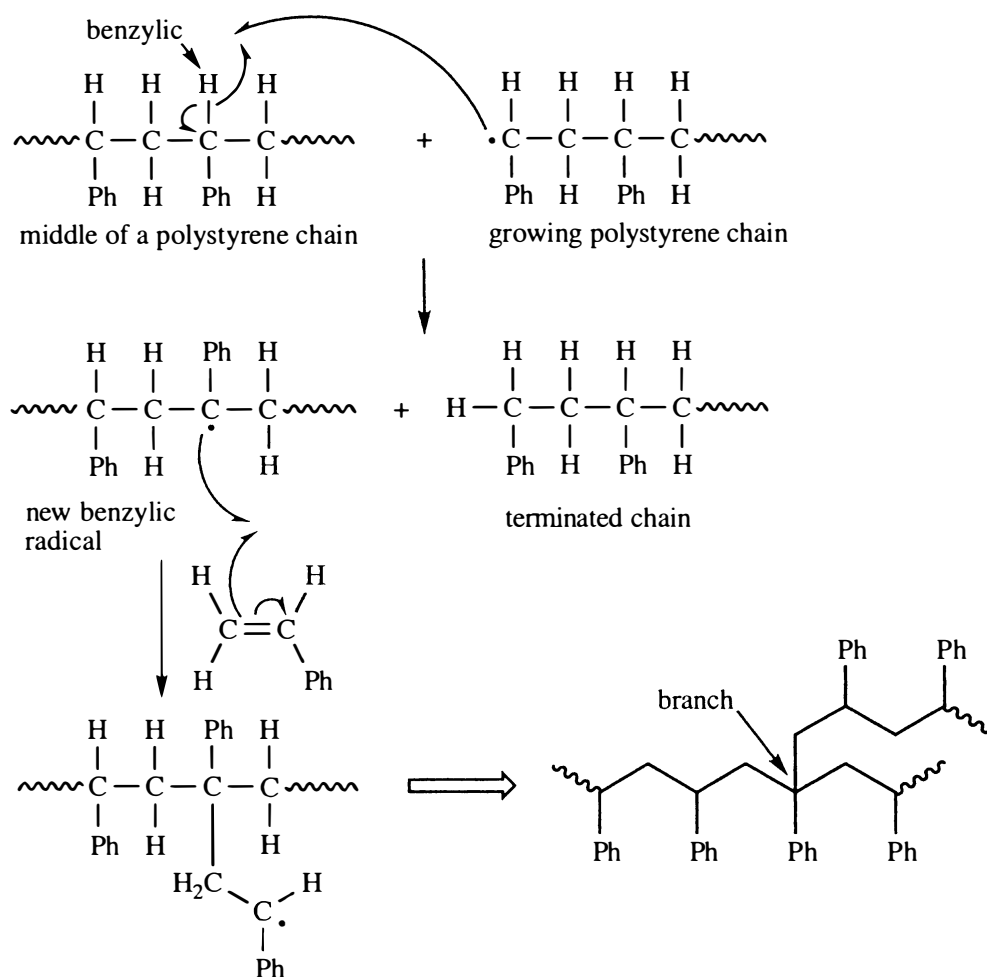
1° radical, and *not* resonance-stabilized—
this orientation is not observed

Orientation of addition always generates the more stable intermediate; the energy difference between a 1° radical (shown above) and a benzylic radical is huge. Moreover, this energy difference accumulates with each repetition of the propagation step. The phenyl substituents must necessarily be on alternating carbons because the orientation of attack is always the same—not a random process.

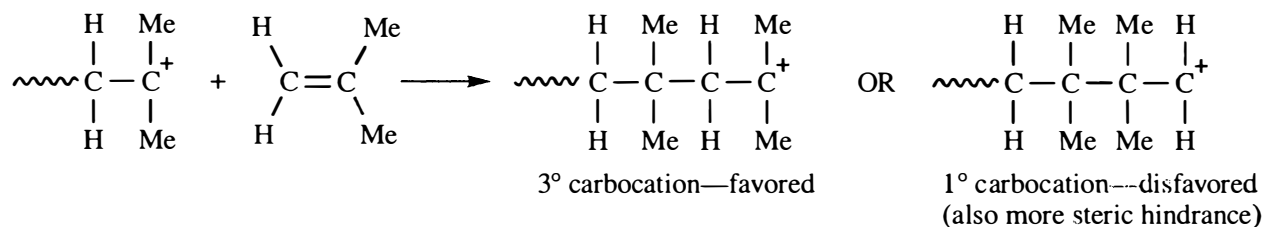
26-2



26-3 The benzylic hydrogen will be abstracted in preference to a 2° hydrogen because the benzylic radical is both 3° and resonance-stabilized, and the 2° radical is neither.

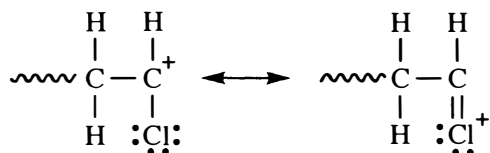


26-4 Addition occurs with the orientation giving the more stable intermediate. In the case of isobutylene, the growing chain will bond at the less substituted carbon to generate the more highly substituted carbocation.



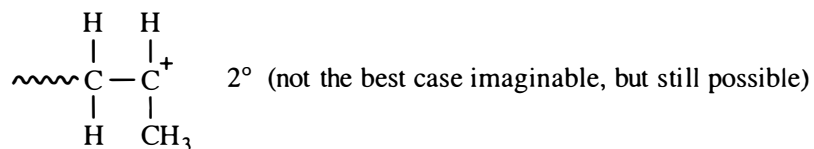
26-5

(a) chlorine can stabilize a carbocation intermediate by resonance

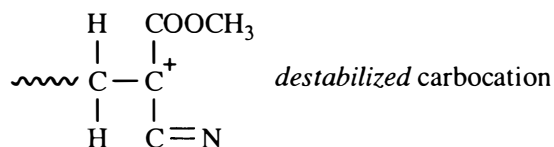


26-5 continued

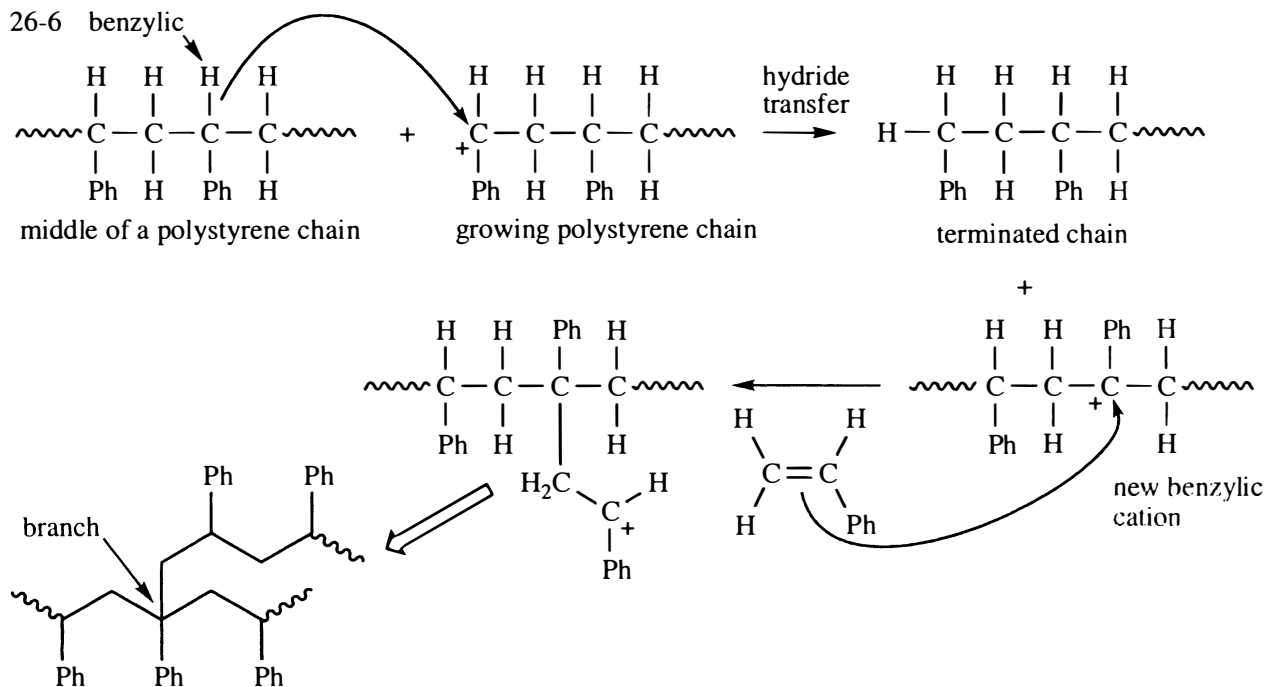
(b) CH_3 can stabilize the carbocation intermediate by induction



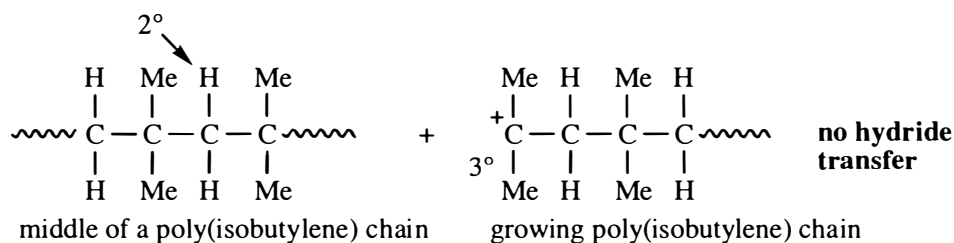
(c) terrible for cationic polymerization: both substituents are electron-withdrawing and would *destabilize* the carbocation intermediate



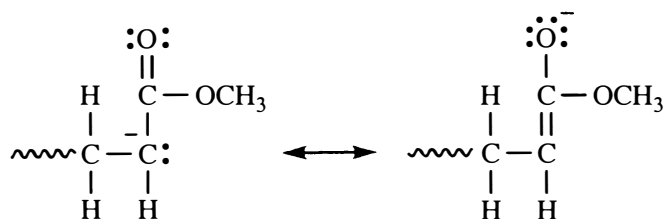
26-6 benzylic



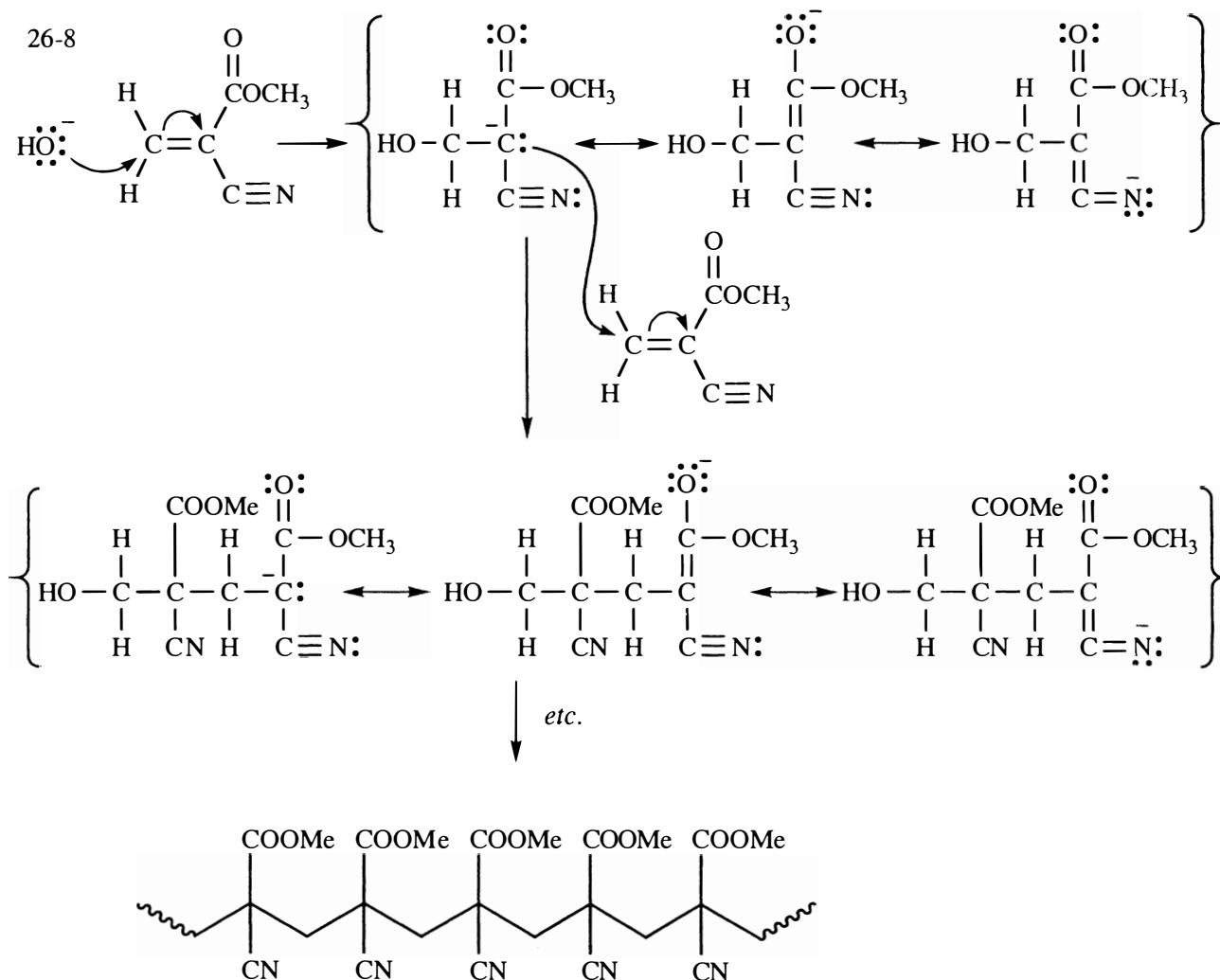
Polystyrene is particularly susceptible to branching because the 3° benzylic cation produced by a hydride transfer is so stable. In poly(isobutylene), there is no hydrogen on the carbon with the stabilizing substituents; any hydride transfer would generate a 2° carbocation at the expense of a 3° carbocation at the end of a growing chain—this is an increase in energy and therefore unfavorable.



26-7



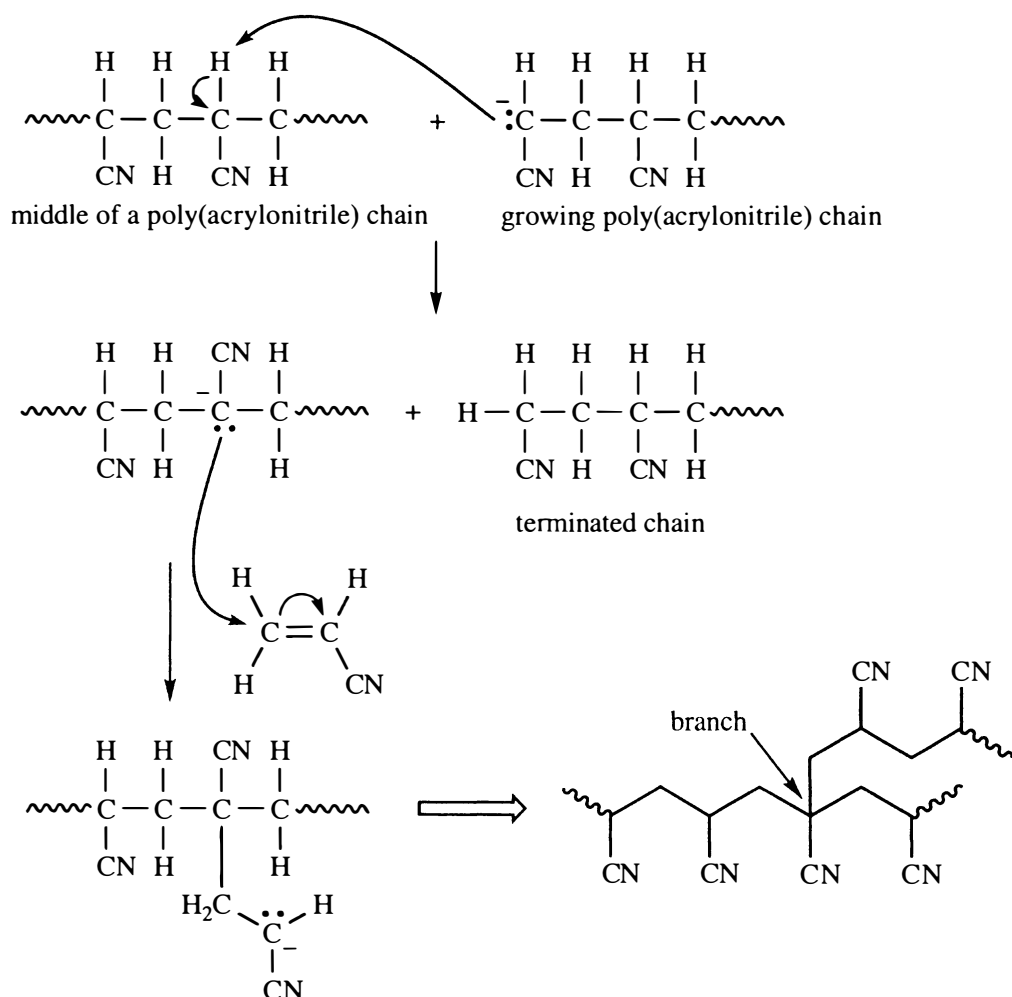
26-8



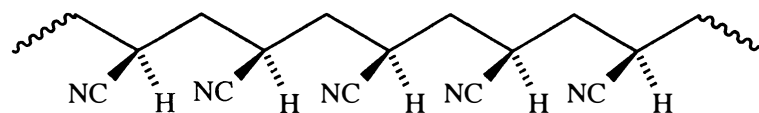
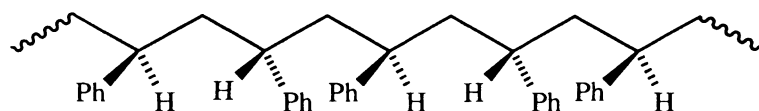
This polymerization goes so quickly because the anionic intermediate is highly resonance stabilized by the carbonyl and the cyano groups. A stable intermediate suggests a low activation energy which translates to a fast reaction.

26-9

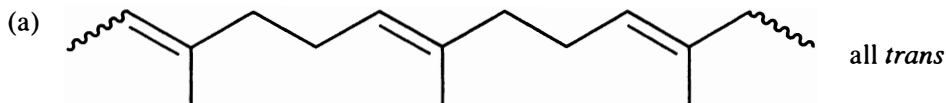
(a)



(b) The chain-branching hydride transfer (from a cationic mechanism) or proton transfer (from an anionic mechanism) ends a less-highly-substituted end of a chain and generates an intermediate on a more-highly-substituted middle of a chain (a 3° carbon in these mechanisms). This stabilizes a carbocation, but greater substitution *destabilizes* a carbanion. Branching can and does happen in anionic mechanisms, but it is less likely than in cationic mechanisms.

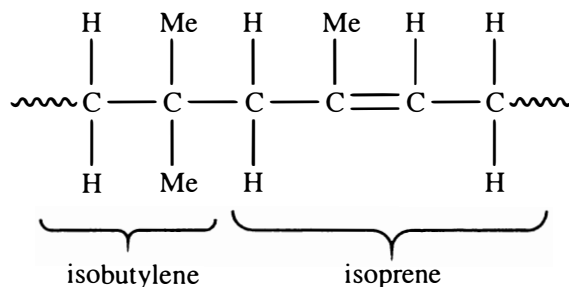
26-10 isotactic poly(acrylonitrile)syndiotactic polystyrene

26-11

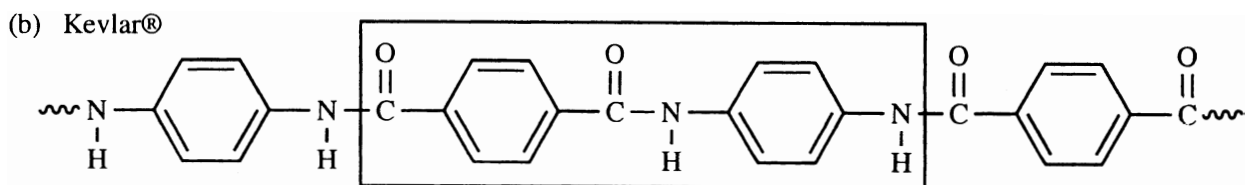
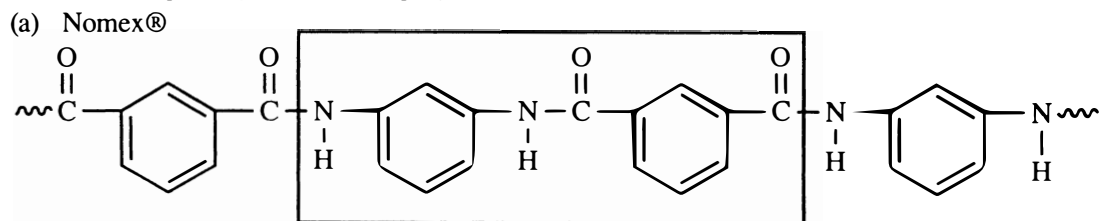


(b) The *trans* double bonds in gutta-percha allow for more ordered packing of the chains, that is, a higher degree of crystallinity. (Recall how *cis* double bonds in fats and oils lower the melting points because the *cis* orientation disrupts the ordering of the packing of the chains.) The more crystalline a polymer is, the less elastic it is.

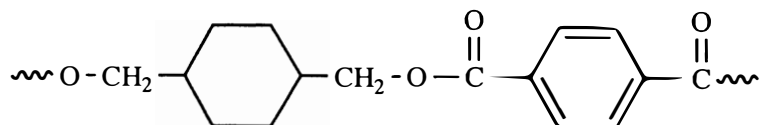
26-12 Whether the alkene is *cis* or *trans* is not specified.



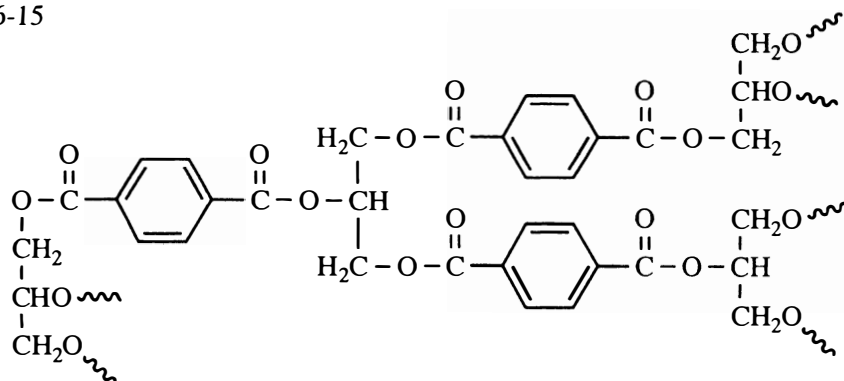
26-13 The repeating unit in each polymer is boxed.



26-14 Kodel® polyester (only one repeating unit shown)

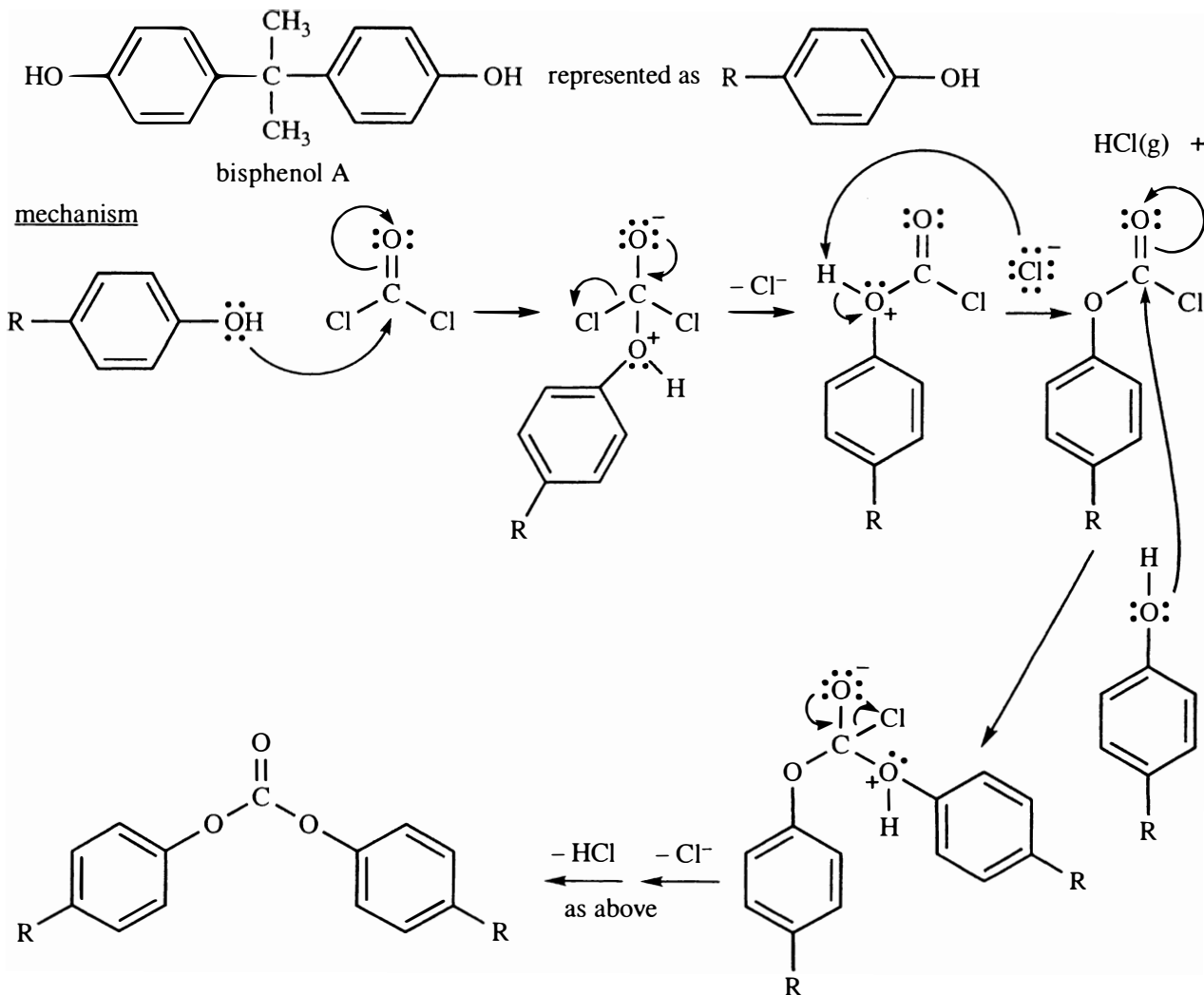


26-15

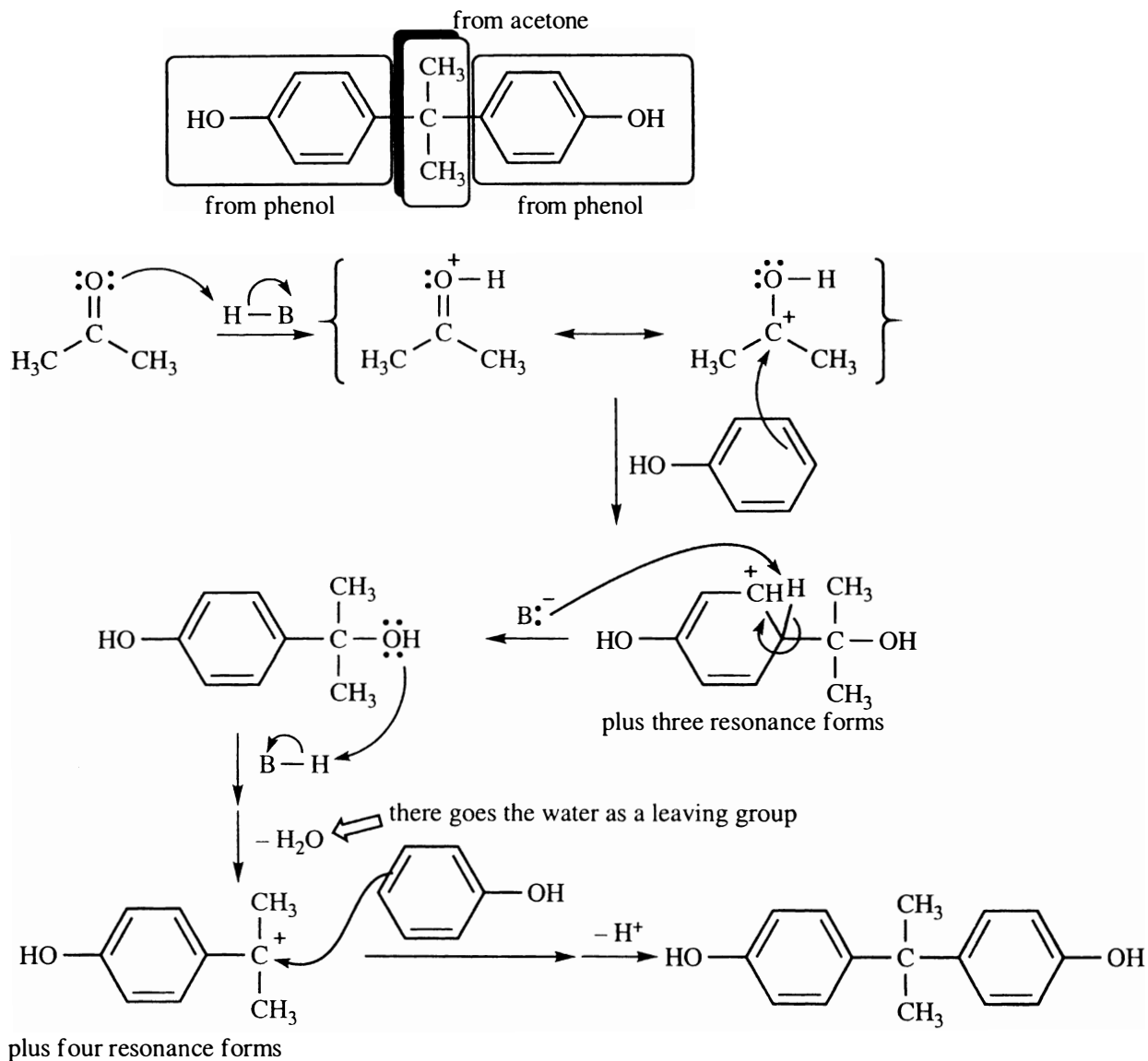


Glycerol is a trifunctional molecule, so not only does it grow in two directions to make a chain, it grows in three directions. All of its chains are cross-linked, forming a three-dimensional lattice with very little motion possible. The more cross-linked the polymer is, the more rigid it is.

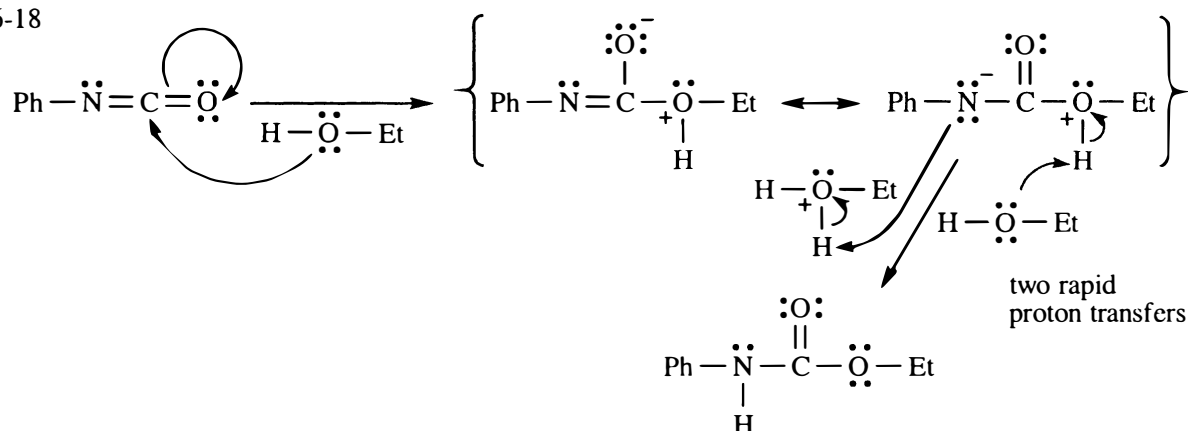
26-16 For simplicity in this problem, bisphenol A will be abbreviated as a substituted phenol.



26-17 Bisphenol A is made by condensing two molecules of phenol with one molecule of acetone, with loss of a molecule of water. This is an electrophilic aromatic substitution (more specifically, a Friedel-Crafts alkylation), and would require an acid catalyst to generate the carbocation. While a Lewis acid could be used, the mechanism below shows a protic acid.

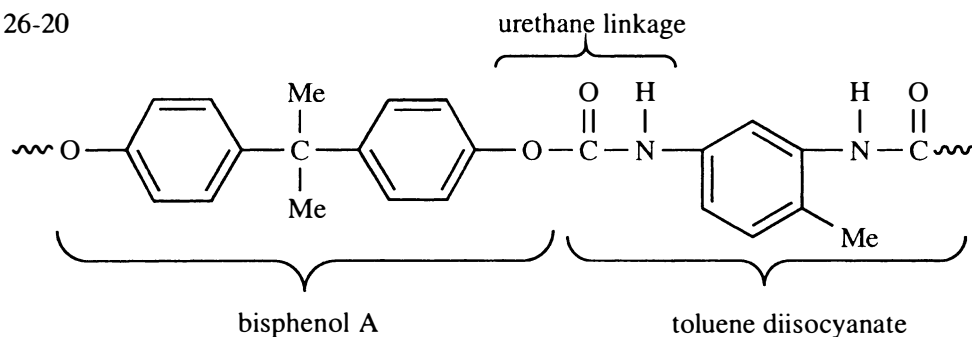


26-18



26-19 Glycerol is a trifunctional alcohol. It uses two of its OH groups in a growing chain. The third OH group cross-links with another chain. The more cross-linked a polymer, the more rigid it is.

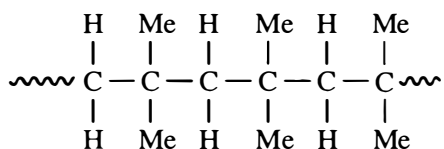
26-20



26-21 Please refer to solution 1-20, page 12 of this Solutions Manual.

26-22

(a)



(b) Polyisobutylene is an addition polymer. No small molecule is lost, so this cannot be a condensation polymer.

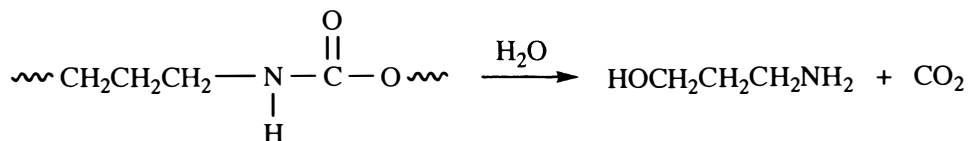
(c) Either cationic polymerization or free-radical polymerization would be appropriate. The carbocation or free-radical intermediate would be 3° and therefore relatively stable. Anionic polymerization would be inappropriate as there is no electron-withdrawing group to stabilize the anion.

26-23

(a) It is a polyurethane.

(b) As with all polyurethanes, it is a condensation polymer.

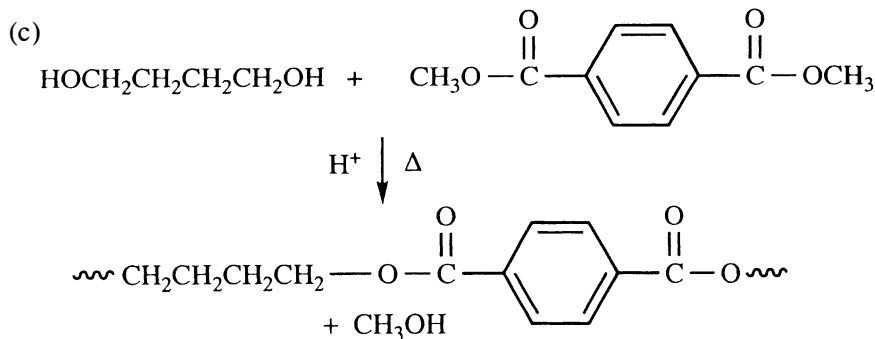
(c)



26-24

(a) It is a polyester.

(b) As with all polyesters, it is a condensation polymer.

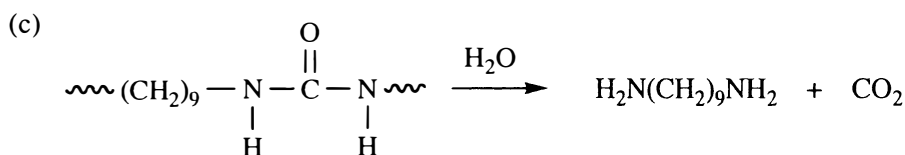


Using the dicarboxylic acid instead of the ester would produce water as the small neutral molecule lost in this condensation.

26-25

(a) Urylon® is a polyurea.

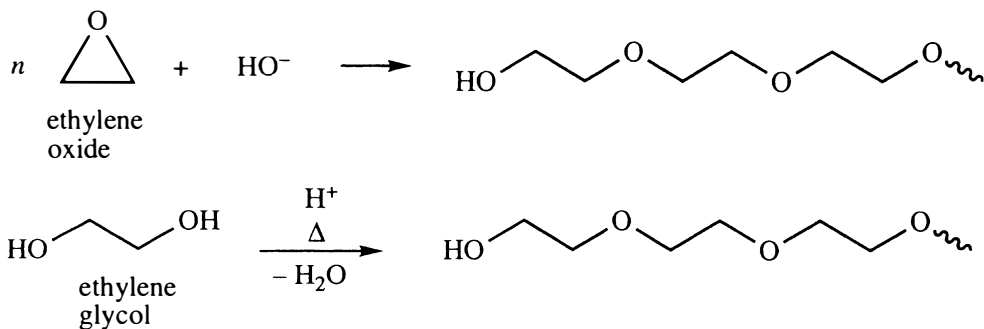
(b) A polyurea is a condensation polymer.



26-26

(a) Polyethylene glycol, abbreviated PEG, is a polyether.

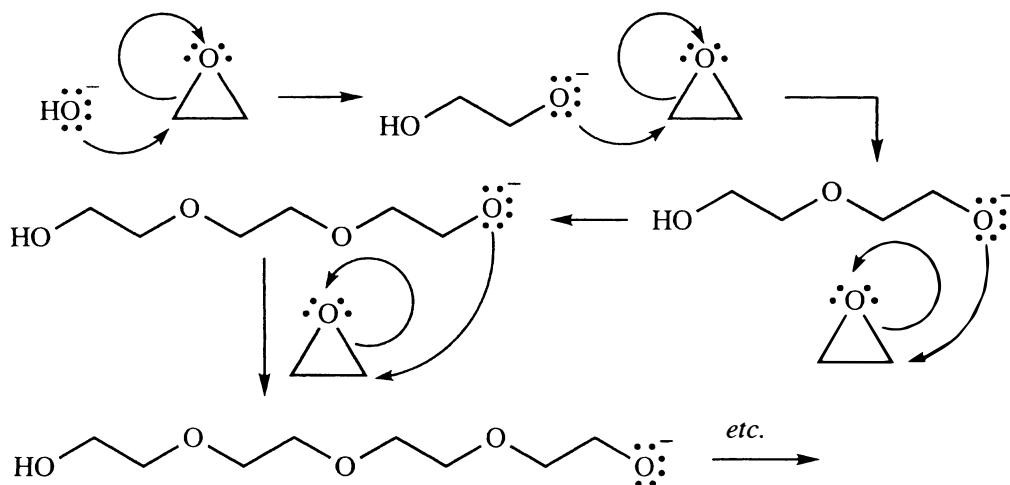
(b) PEG is usually made from ethylene oxide (first reaction shown). In theory, PEG could also be made by intermolecular dehydration of ethylene glycol (second reaction shown), but the yields are low and the chains are short.



(c) Basic catalysts are most likely as they open the epoxide to generate a new nucleophile. Acid catalysts are possible but they risk dehydration and ether cleavage.

26-26 continued

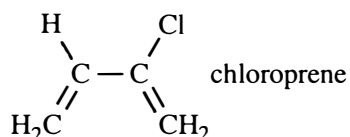
(d) Mechanism of ethylene oxide polymerization (showing hydroxide as the base):



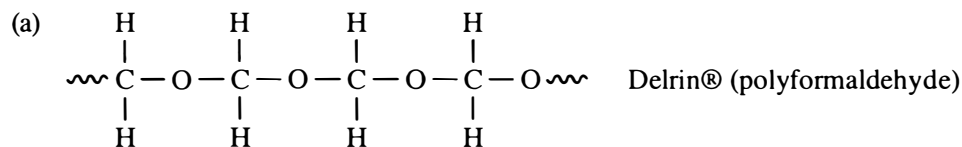
26-27

(a) Polychloroprene (Neoprene®) is an addition polymer.

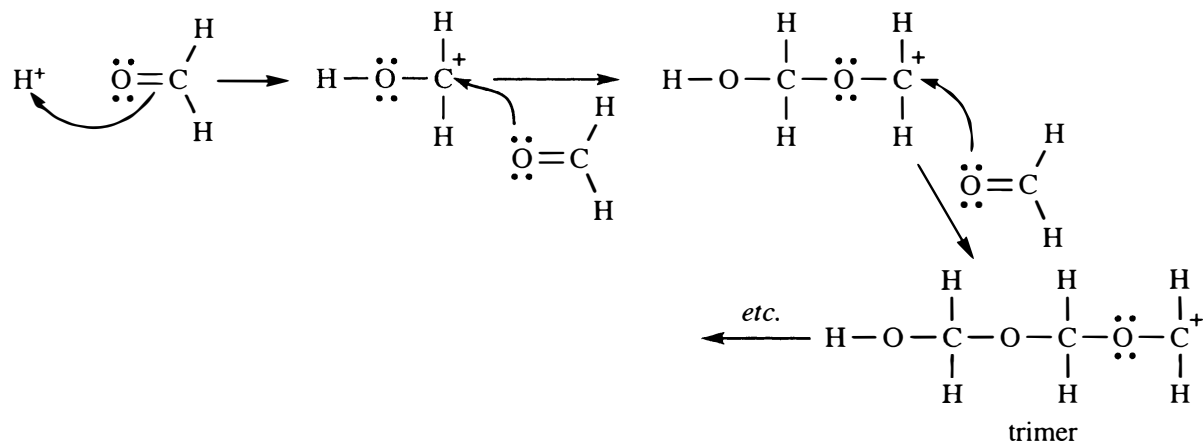
(b) Polychloroprene comes from the diene, chloroprene, just as natural rubber comes from isoprene:



26-28



(b) All of these intermediates are resonance-stabilized.



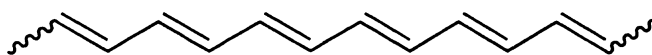
(c) Delrin® is an addition polymer; instead of adding across the double bond of an alkene, addition occurs across the double bond of a carbonyl group.

26-29

(a) *cis*



trans

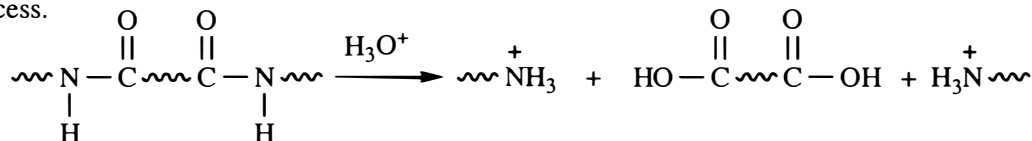


(b) Each structure has a fully conjugated chain. It is reasonable to expect electrons to be able to be transferred through the π system, just as resonance effects can work over long distances through conjugated systems.

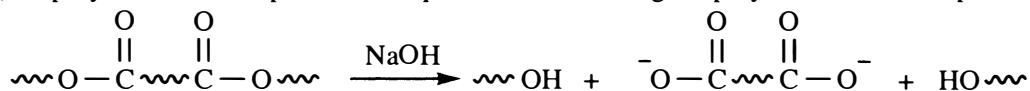
(c) It is not surprising that the conductivity is directional. Electrons must flow along the π system of the chain, so if the chains were aligned, conductivity would be greater in the direction parallel to the polymer chains. (It is possible, though less likely, that electrons could pass from the π system of one chain to the π system of another, that is, perpendicular to the direction of the chain; we would expect reduced conductivity in that direction.)

26-30

(a) A Nylon is a polyamide. Amides can be hydrolyzed in aqueous acid, cleaving the polymer chain in the process.

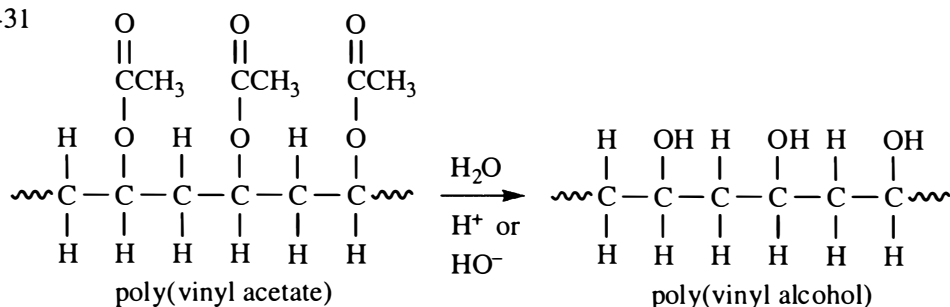


(b) A polyester can be saponified in aqueous base, cleaving the polymer chain in the process.



26-31

(a)

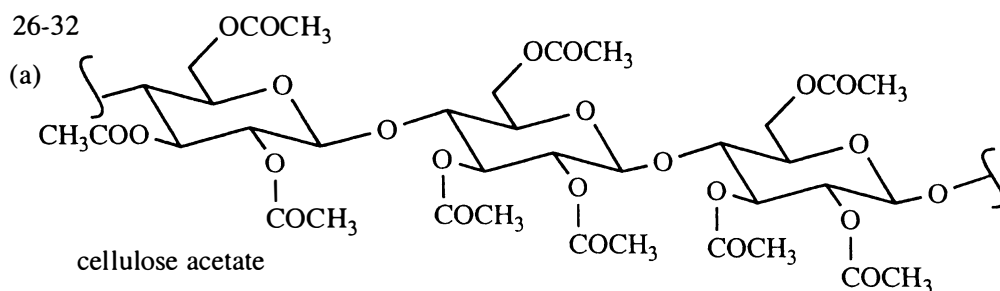


(b) A polyester is a condensation polymer in which monomer units are linked through ester groups as part of the polymer chain. Poly(vinyl acetate) is really a substituted polyethylene, an **addition** polymer, with only carbons in the chain; the ester groups are in the side chains, not in the polymer backbone.

(c) Hydrolysis of the esters in poly(vinyl acetate) does not affect the chain because the ester groups do not occur in the chain as they do in Dacron®.

(d) Vinyl alcohol cannot be polymerized because it is unstable, tautomerizing to acetaldehyde.

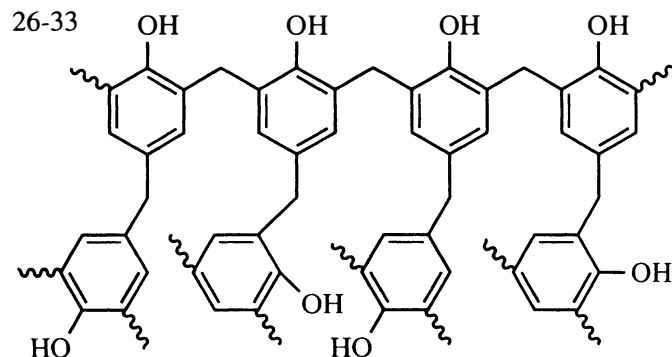




(b) Cellulose has three OH groups per glucose monomer, which form hydrogen bonds with other polar groups. Transforming these OH groups into acetates makes the polymer much less polar and therefore more soluble in organic solvents.

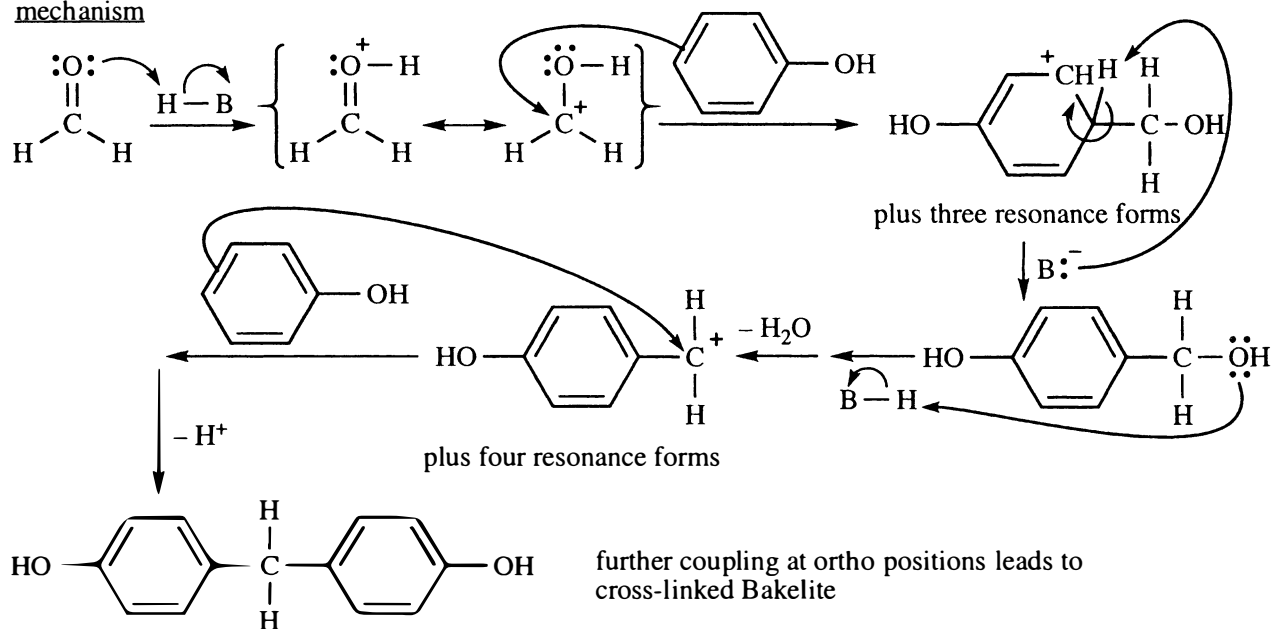
(c) The acetone dissolved the cellulose acetate in the fibers. As the acetone evaporated, the cellulose acetate remained but no longer had the fibrous, woven structure of cloth. It recrystallized as white fluff.

(d) Any article of clothing made from synthetic fibers is susceptible to the ravages of organic solvents. Solvent splashes leave dimples or blotches on Corfam shoes. (Yet, Corfam shoes could still provide protection for the toenail polish!)

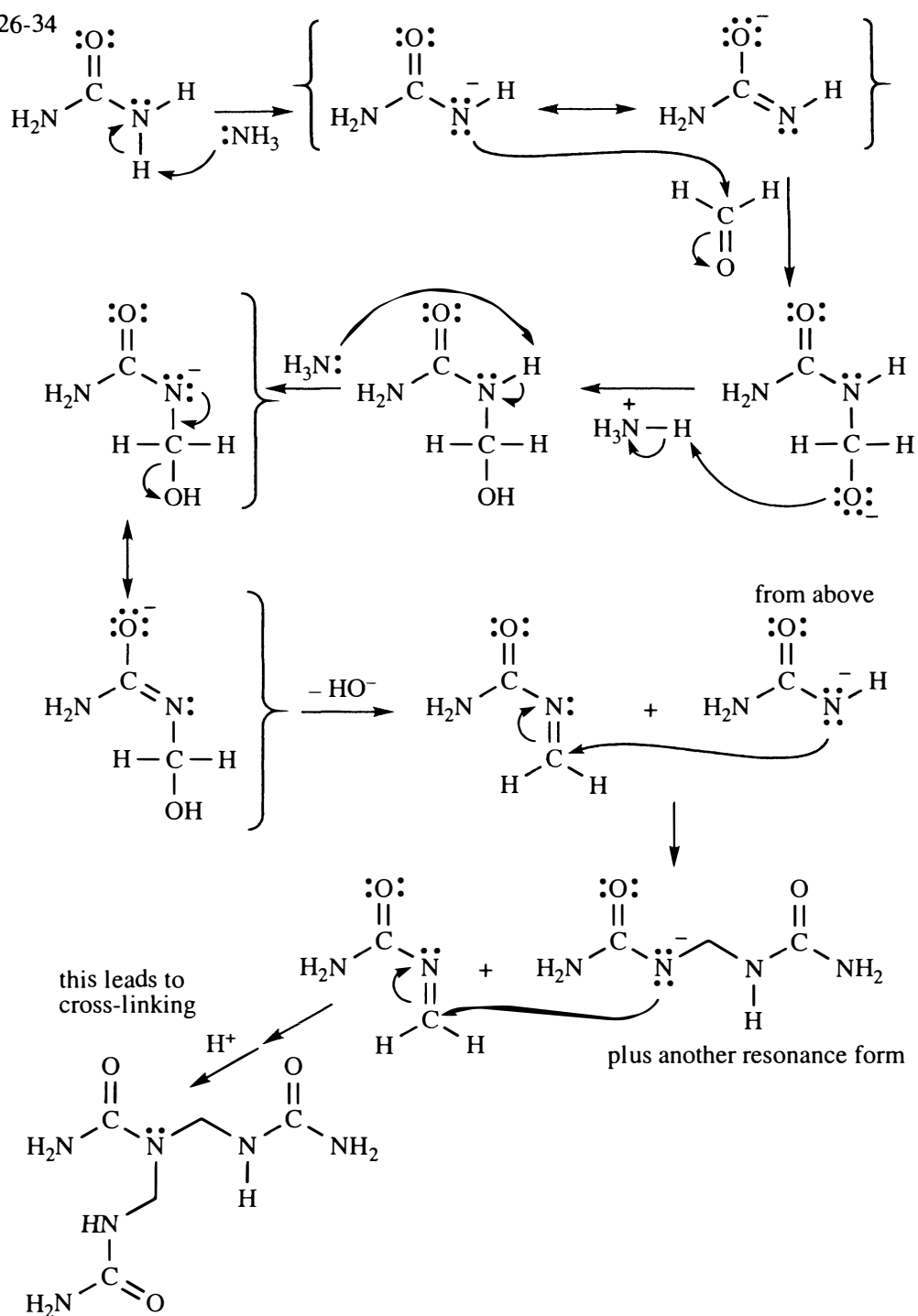


Bakelite is highly cross-linked through the ortho and para positions of phenol; each phenol can form a chain at two ring positions, then form a branch at the third position.

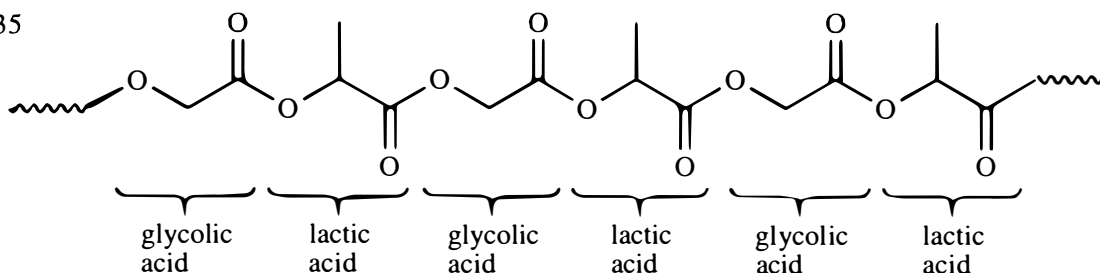
mechanism



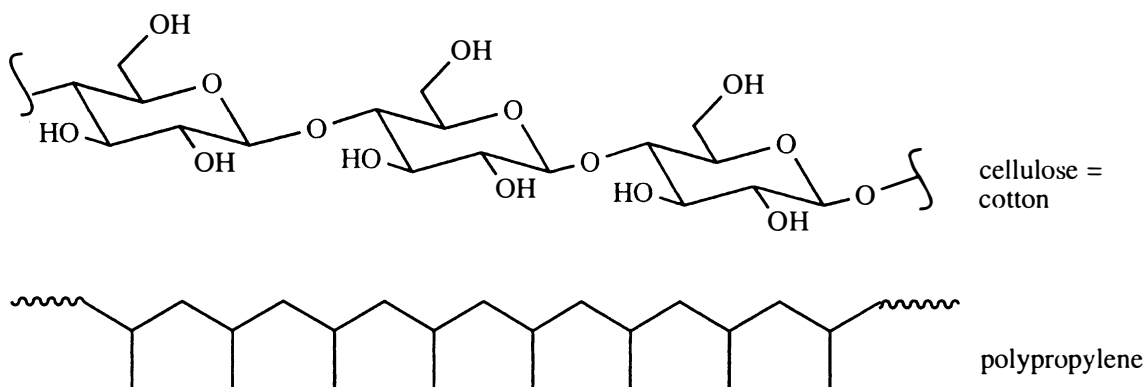
26-34



26-35



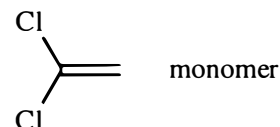
26-36



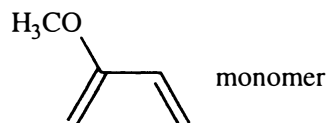
As we have seen repeatedly through this presentation of organic chemistry, physical and chemical behavior depend on *structure*. The structure of cotton, i.e. cellulose, has multiple oxygen atoms that form hydrogen bonds with water. When cotton gets wet, it holds onto the water tightly, as you have seen if you have put cotton clothes in a clothes dryer—it takes a long time to dry. Polypropylene is a hydrocarbon with no hydrogen bonding groups; the fiber feels dry because it cannot hold the water the way cotton can. Athletic garments are increasingly using polypropylene because they allow evaporation and cooling during periods of exertion; cotton is just the opposite.

26-37

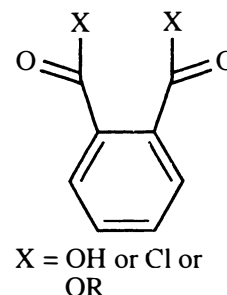
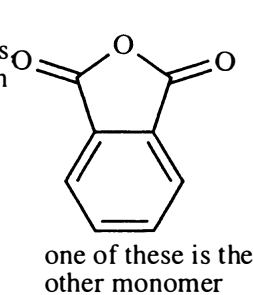
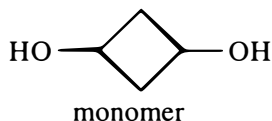
(a) This addition polymer is called polyvinylidene chloride, trade name Saran®. It could be made by any of the three mechanism types: radical, cationic, or anionic.



(b) When the substituent is on every fourth carbon, and one double bond in the chain in every 4-carbon unit, the polymer must come from addition across a diene, probably under cationic conditions.

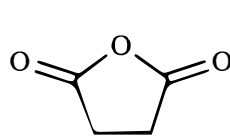
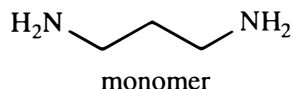


(c) This polyester is a condensation polymer of two monomers: a diol and a derivative of phthalic acid, either the anhydride, an ester, the acid chloride, or the acid itself. Heating the monomers will make the polymer; no catalyst is required if done at high temperature.

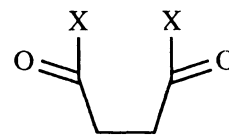


26-37 continued

(d) This polyamide (Nylon) is a condensation polymer made from two monomers, a diamine and a derivative of succinic acid, either the anhydride, an ester, the acid chloride, or the acid itself. Heating the monomers will make the polymer; no catalyst is required if done at high temperature.



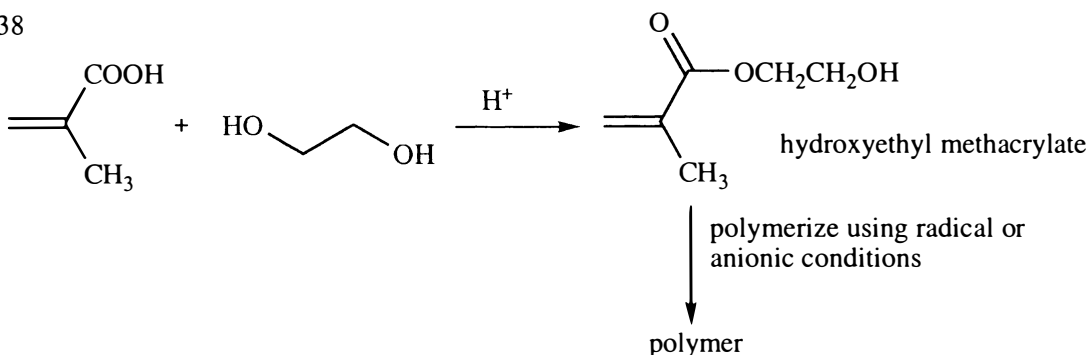
one of these is the other monomer



X = OH or Cl or OR

26-38

(a)



(b) This polymer has a few properties that make it useful as the material in soft, extended-wear contact lenses. First, carboxylic acids usually are crystalline solids with high melting points, but esters and alcohols are low melting, often liquids, so the polymer with this ester is softer than the carboxylic acid or even the methyl ester. (The methyl ester, polymethyl methacrylate or Plexiglas, was the first material used in the original hard contact lenses.) Second, the ability of the free OH to form hydrogen bonds with water makes the contact lens more fluid and less irritating to the cornea. Third, a hidden advantage but very important for ocular health: the fluidity of the contact lens also permits oxygen to go through the lens. Because the cornea does not have a large blood flow, it needs to absorb oxygen from the air to maintain its health, and this enhanced gas permeability permits the contact lens to be worn for days at a time without compromising the health of the cornea. Thanks, polymers!

Note to the student: BON VOYAGE!
I hope you have enjoyed your travels
through organic chemistry.

Jan Simek

Appendix 1—Summary of IUPAC Nomenclature of Organic Compounds

Introduction

The purpose of the IUPAC system of nomenclature is to establish an international standard of naming compounds to facilitate communication. The goal of the system is to give each structure a unique and unambiguous name, and to correlate each name with a unique and unambiguous structure.

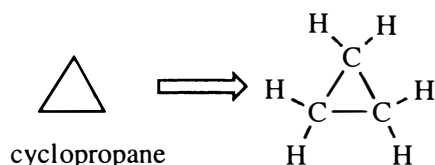
I. Fundamental Principle

IUPAC nomenclature is based on naming a molecule's longest chain of carbons connected by single bonds, whether in a continuous chain or in a ring. All deviations, either multiple bonds or atoms other than carbon and hydrogen, are indicated by prefixes or suffixes according to a specific set of priorities.

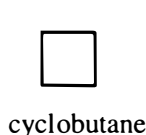
II. Alkanes and Cycloalkanes (also called "aliphatic" compounds)

Alkanes are the family of saturated hydrocarbons, that is, molecules containing carbon and hydrogen connected by single bonds only. These molecules can be in continuous chains (called linear or acyclic), or in rings (called cyclic or alicyclic). The names of alkanes and cycloalkanes are the root names of organic compounds. Beginning with the five-carbon alkane, the number of carbons in the chain is indicated by the Greek or Latin prefix. Rings are designated by the prefix "cyclo". (In the geometrical symbols for rings, each apex represents a carbon with the number of hydrogens required to fill its valence.)

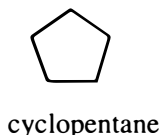
C ₁	CH ₄	methane	C ₁₂	CH ₃ [CH ₂] ₁₀ CH ₃	dodecane
C ₂	CH ₃ CH ₃	ethane	C ₁₃	CH ₃ [CH ₂] ₁₁ CH ₃	tridecane
C ₃	CH ₃ CH ₂ CH ₃	propane	C ₁₄	CH ₃ [CH ₂] ₁₂ CH ₃	tetradecane
C ₄	CH ₃ [CH ₂] ₂ CH ₃	butane	C ₂₀	CH ₃ [CH ₂] ₁₈ CH ₃	icosane
C ₅	CH ₃ [CH ₂] ₃ CH ₃	pentane	C ₂₁	CH ₃ [CH ₂] ₁₉ CH ₃	heneicosane
C ₆	CH ₃ [CH ₂] ₄ CH ₃	hexane	C ₂₂	CH ₃ [CH ₂] ₂₀ CH ₃	docosane
C ₇	CH ₃ [CH ₂] ₅ CH ₃	heptane	C ₂₃	CH ₃ [CH ₂] ₂₁ CH ₃	tricosane
C ₈	CH ₃ [CH ₂] ₆ CH ₃	octane	C ₃₀	CH ₃ [CH ₂] ₂₈ CH ₃	triacontane
C ₉	CH ₃ [CH ₂] ₇ CH ₃	nonane	C ₃₁	CH ₃ [CH ₂] ₂₉ CH ₃	hentriacontane
C ₁₀	CH ₃ [CH ₂] ₈ CH ₃	decane	C ₄₀	CH ₃ [CH ₂] ₃₈ CH ₃	tetracontane
C ₁₁	CH ₃ [CH ₂] ₉ CH ₃	undecane	C ₅₀	CH ₃ [CH ₂] ₄₈ CH ₃	pentacontane



cyclopropane



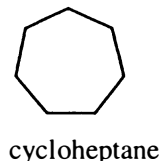
cyclobutane



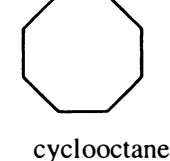
cyclopentane



cyclohexane



cycloheptane



cyclooctane

The IUPAC system of nomenclature is undergoing many changes, most notably in the placement of position numbers. The new system places the position number close to the functional group designation; however, you should be able to use and recognize names in either the old or the new style. Ask your instructor which system to use.

III. Nomenclature of Molecules Containing Substituents and Functional Groups

A. Priorities of Substituents and Functional Groups

LISTED HERE FROM HIGHEST TO LOWEST PRIORITY, except that the substituents within Group C have equivalent priority.

Group A—Functional Groups Named By Prefix Or Suffix

<u>Functional Group</u>	<u>Structure</u>	<u>Prefix</u>	<u>Suffix</u>
Carboxylic Acid	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{OH} \end{array}$	carboxy-	-oic acid (-carboxylic acid)
Aldehyde	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{H} \end{array}$	oxo- (formyl)	-al (carbaldehyde)
Ketone	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{R} \end{array}$	oxo-	-one
Alcohol	$\text{R}-\text{O}-\text{H}$	hydroxy-	-ol
Amine	$\text{R}-\text{N} \begin{array}{l} \diagup \\ \diagdown \end{array}$	amino-	-amine

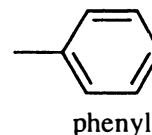
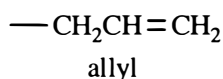
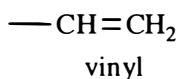
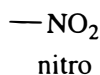
Group B—Functional Groups Named By Suffix Only

<u>Functional Group</u>	<u>Structure</u>	<u>Prefix</u>	<u>Suffix</u>
Alkene	$\begin{array}{c} \diagup \quad \diagdown \\ \text{C}=\text{C} \\ \diagdown \quad \diagup \end{array}$	-----	-ene
Alkyne	$-\text{C}\equiv\text{C}-$	-----	-yne

Group C—Substituent Groups Named By Prefix Only

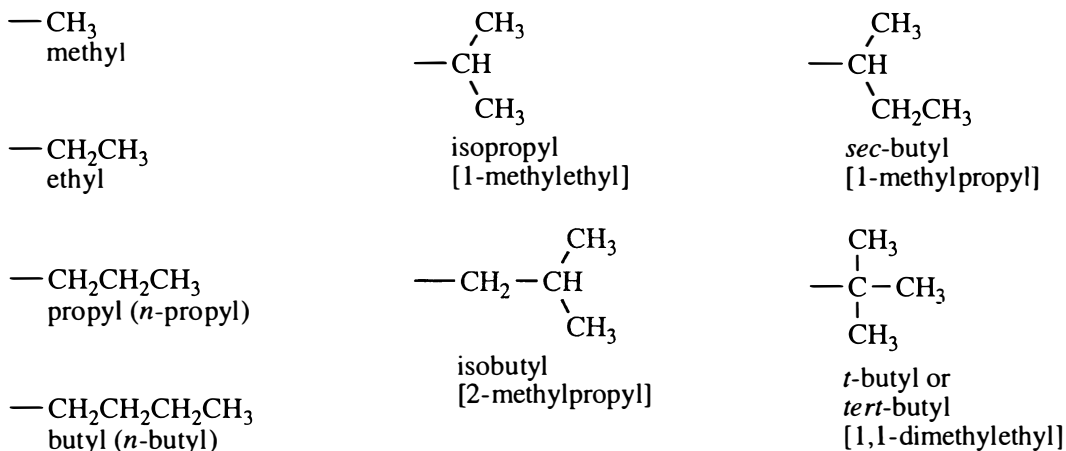
<u>Substituent</u>	<u>Structure</u>	<u>Prefix</u>	<u>Suffix</u>
Alkyl (see next page)	$\text{R}-$	alkyl-	-----
Alkoxy	$\text{R}-\text{O}-$	alkoxy-	-----
(alkoxy groups take the name of the alkyl group, like methyl or ethyl, drop the "yl", and add "oxy"; CH_3O is methoxy; $\text{CH}_3\text{CH}_2\text{O}$ is ethoxy)			
Halogen	$\begin{array}{l} \text{F}- \\ \text{Cl}- \\ \text{Br}- \\ \text{I}- \end{array}$	fluoro- chloro- bromo- iodo-	----- ----- ----- -----

Miscellaneous substituents and their prefixes



Appendix 1, Summary of IUPAC Nomenclature, continued

Common alkyl groups—replace "ane" ending of alkane name with "yl". Alternate names for complex substituents are given in brackets.



B. Naming Substituted Alkanes and Cycloalkanes—Group C Substituents Only

Organic compounds containing substituents from Group C are named following this sequence of steps, as indicated on the examples below:

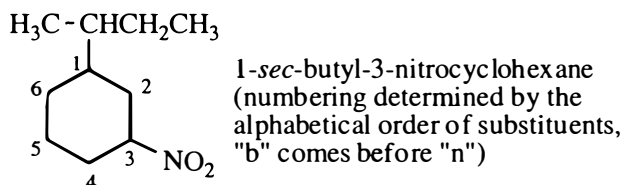
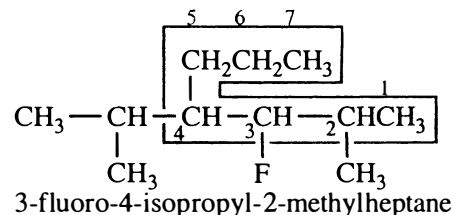
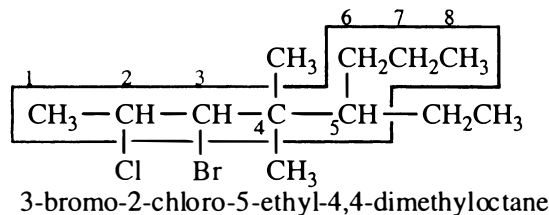
•Step 1. Find the longest continuous carbon chain. Determine the root name for this parent chain. In cyclic compounds, the ring is usually considered the parent chain, unless it is attached to a longer chain of carbons; indicate a ring with the prefix "cyclo" before the root name. (When there are two longest chains of equal length, use the chain with the greater number of substituents.)

•Step 2. Number the chain in the direction such that the position number of the first substituent is the smaller number. If the first substituents have the same number, then number so that the second substituent has the smaller number, *etc.*

•Step 3. Determine the name and position number of each substituent. (A substituent on a nitrogen is designated with an "N" instead of a number; see Section III.D.1. below.)

•Step 4. Indicate the number of identical groups by the prefixes di, tri, tetra, *etc.*

•Step 5. Place the position numbers and names of the substituent groups, in alphabetical order, before the root name. In alphabetizing, ignore prefixes like *sec*-, *tert*-, di, tri, *etc.*, but include iso and cyclo. Always include a position number for each substituent, regardless of redundancies.

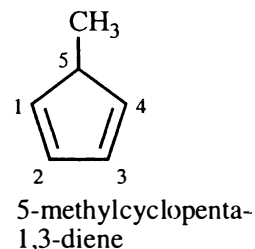
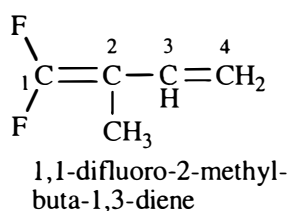
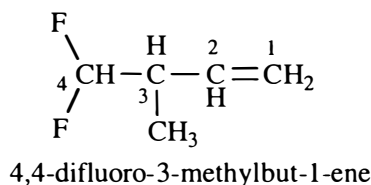


Appendix 1, Summary of IUPAC Nomenclature, continued

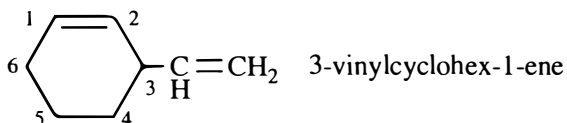
C. Naming Molecules Containing Functional Groups from Group B—Suffix Only

1. Alkenes—Follow the same steps as for alkanes, except:

- Number the chain of carbons *that includes the C=C* so that the C=C has the lower position number, since it has a higher priority than any substituents;
- Change "ane" to "ene" and assign a position number to the first carbon of the C=C; place the position number just before the name of functional group(s);
- Designate geometrical isomers with a *cis,trans* or *E,Z* prefix.



Special case: When the chain cannot include an alkene, a substituent name is used. See Section V.A.2.a.

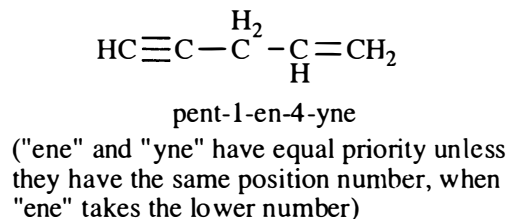
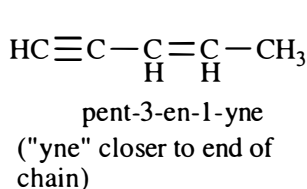
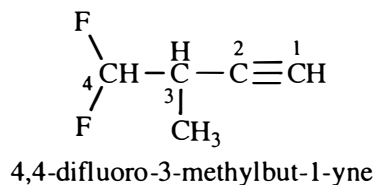


Numbering must be on EITHER a ring OR a chain, but not both.

2. Alkynes—Follow the same steps as for alkanes, except:

- Number the chain of carbons *that includes the C≡C* so that the alkyne has the lower position number;
- Change "ane" to "yne" and assign a position number to the first carbon of the C≡C; place the position number just before the name of functional group(s).

Note: The Group B functional groups (alkene and alkyne) are considered to have equal priority: in a molecule with both an ene and an yne, whichever is closer to the end of the chain determines the direction of numbering. In the case where each would have the same position number, the alkene takes the lower number. In the name, "ene" comes before "yne" because of alphabetization.



(Notes: 1. An "e" is dropped if the letter following it is a vowel: "pent-3-en-1-yne", not "pent-3-ene-1-yne". 2. An "a" is added if inclusion of di, tri, *etc.*, would put two consonants together: "buta-1,3-diene", not "but-1,3-diene".)

D. Naming Molecules Containing Functional Groups from Group A—Prefix or Suffix

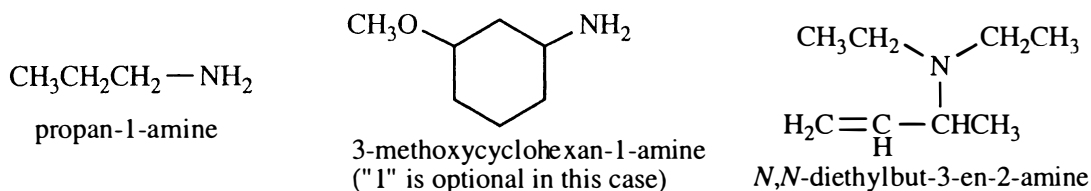
In naming molecules containing one or more of the functional groups in Group A, the group of highest priority is indicated by suffix; the others are indicated by prefix, with priority equivalent to any other substituents. The table in Section III.A. defines the priorities; they are discussed on the following pages in order of increasing priority.

Appendix 1, Summary of IUPAC Nomenclature, continued

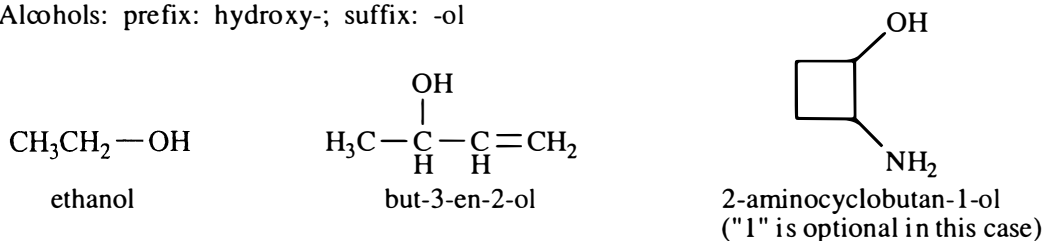
Now that the functional groups and substituents from Groups A, B, and C have been described, a modified set of steps for naming organic compounds can be applied to all simple structures:

- Step 1. Find the highest priority functional group. Determine and name the longest continuous carbon chain that includes this group.
- Step 2. Number the chain so that the highest priority functional group is assigned the lower number. (The number "1" is often omitted when there is no confusion about where the group must be. Aldehydes and carboxylic acids must be at the first carbon of a chain, so a "1" is rarely used with those functional groups.)
- Step 3. If the carbon chain includes multiple bonds (Group B), replace "ane" with "ene" for an alkene or "yne" for an alkyne. Designate the position of the multiple bond with the number of the first carbon of the multiple bond.
- Step 4. If the molecule includes Group A functional groups, replace the last "e" with the suffix of the highest priority functional group, and include its position number just before the name of the highest priority functional group.
- Step 5. Indicate all Group C substituents, and Group A functional groups of lower priority, with a prefix. Place the prefixes, with appropriate position numbers, in alphabetical order before the root name.

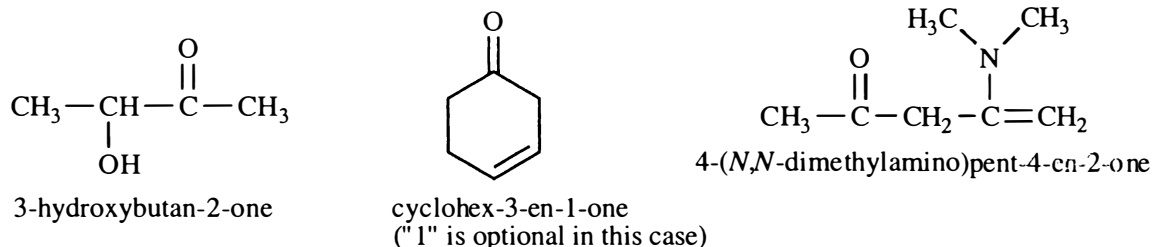
1. Amines: prefix: amino-; suffix: -amine—substituents on nitrogen denoted by "N"



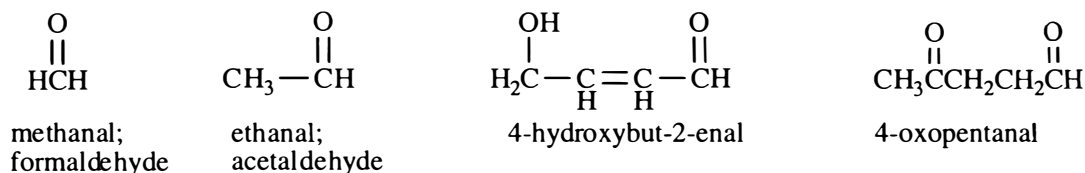
2. Alcohols: prefix: hydroxy-; suffix: -ol



3. Ketones: prefix: oxo-; suffix: -one (pronounced "own")

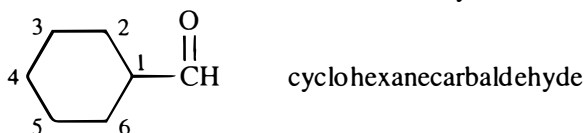


4. Aldehydes: prefix: oxo-, or formyl- ($\text{O}=\text{CH}-$); suffix: -al (abbreviation: $-\text{CHO}$)
An aldehyde can only be on carbon 1, so the "1" is generally omitted from the name.



Appendix 1, Summary of IUPAC Nomenclature, continued

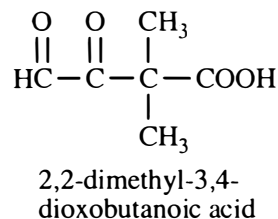
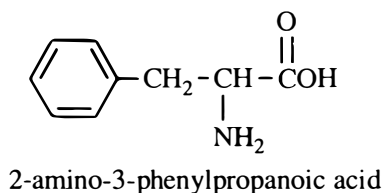
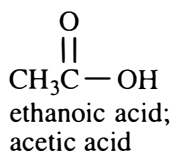
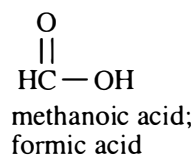
Special case: When the chain cannot include the carbon of the aldehyde, the suffix "carbaldehyde" is used:



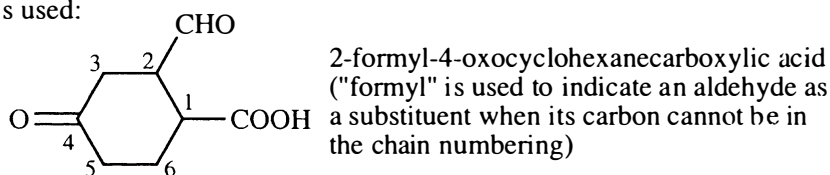
5. Carboxylic Acids: prefix: carboxy-; suffix: -oic acid (abbreviation: —COOH)

A carboxylic acid can only be on carbon 1, so the "1" is generally omitted from the name.

(Note: Chemists traditionally use, and IUPAC accepts, the names "formic acid" and "acetic acid" in place of "methanoic acid" and "ethanoic acid".)



Special case: When the chain numbering cannot include the carbon of the carboxylic acid, the suffix "carboxylic acid" is used:

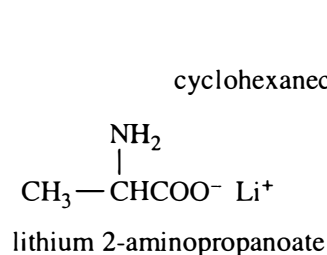


E. Naming Carboxylic Acid Derivatives

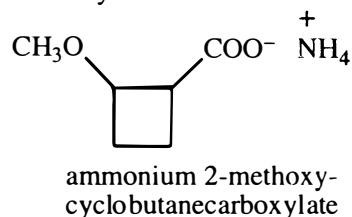
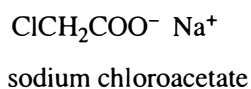
The six common groups derived from carboxylic acids are, in decreasing priority after carboxylic acids: salts, anhydrides, esters, acyl halides, amides, and nitriles.

1. Salts of Carboxylic Acids

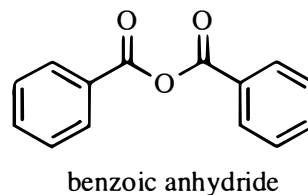
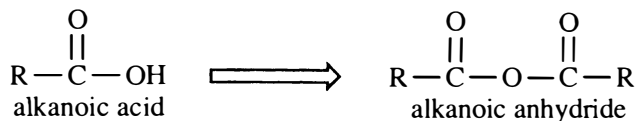
Salts are named with cation first, followed by the anion name of the carboxylic acid, where "ic acid" is replaced by "ate" :



acetic acid	becomes	acetate
butanoic acid	becomes	butanoate
cyclohexanecarboxylic acid	becomes	cyclohexanecarboxylate



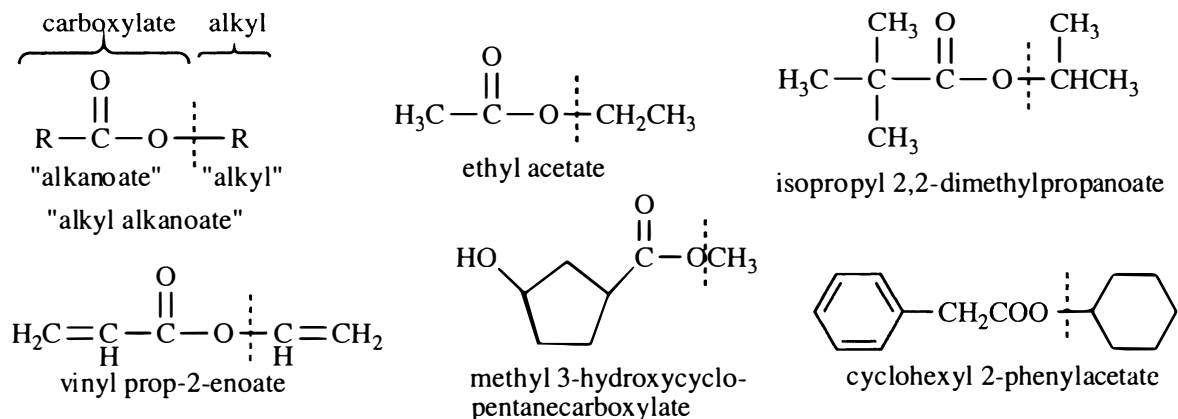
2. Anhydrides: "oic acid" is replaced by "oic anhydride"



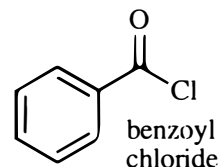
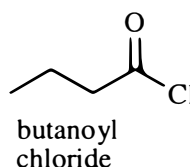
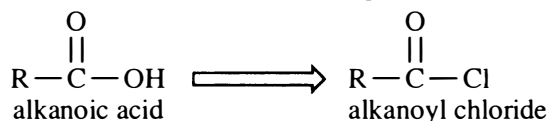
Appendix 1, Summary of IUPAC Nomenclature, continued

3. Esters

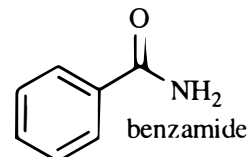
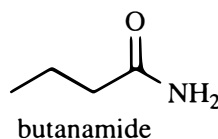
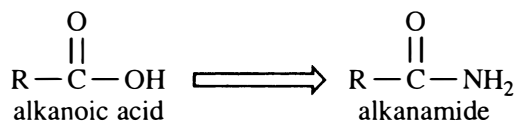
Esters are named as "organic salts" that is, the alkyl name comes first, followed by the name of the carboxylate anion. (common abbreviation: —COOR)



4. Acyl Halides: "oic acid" is replaced by "oyl halide"

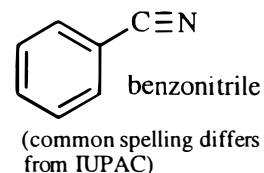
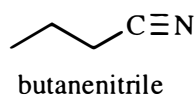
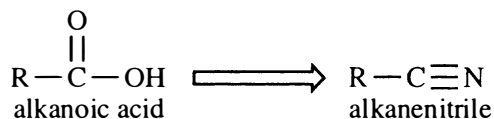


5. Amides: "oic acid" is replaced by "amide"



Amides are notable for their role in biochemistry, i.e., the special amide bond between two amino acids is called a peptide bond.

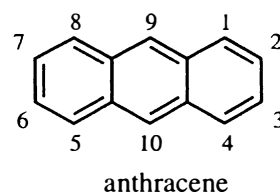
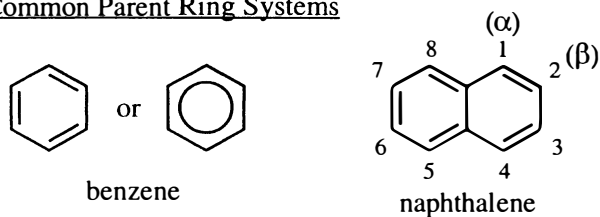
6. Nitriles: "oic acid" is replaced by "nitrile"



IV. Nomenclature of Aromatic Compounds

"Aromatic" compounds are those derived from benzene and similar ring systems. As with aliphatic nomenclature described above, the process is: determining the root name of the parent ring; determining priority, name, and position number of substituents; and assembling the name in alphabetical order. *Functional group priorities are the same in aliphatic and aromatic nomenclature.* See p. 676 for the list of priorities.

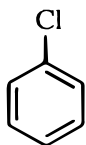
A. Common Parent Ring Systems



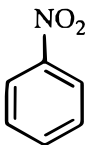
Appendix 1, Summary of IUPAC Nomenclature, continued

B. Monosubstituted Benzenes

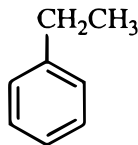
1. Most substituents keep their designation, followed by the word "benzene":



chlorobenzene

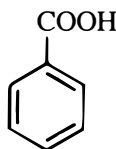


nitrobenzene

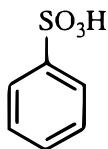


ethylbenzene

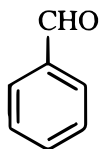
2. Some common substituents change the root name of the ring. IUPAC accepts these as root names, listed here in decreasing priority (same as Group A, p. 676):



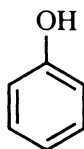
benzoic acid



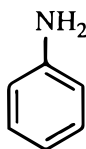
benzenesulfonic acid



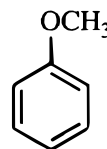
benzaldehyde



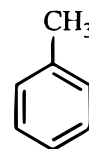
phenol



aniline



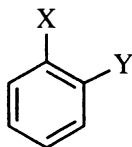
anisole



toluene

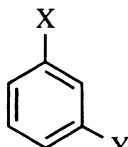
C. Disubstituted Benzenes

1. Designation of substitution—only three possibilities:

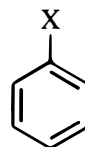


common:
IUPAC:

ortho-
1,2- (*o-*)

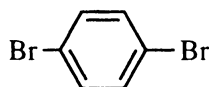


meta-
1,3- (*m-*)

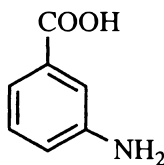


para-
1,4- (*p-*)

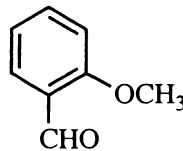
2. Naming disubstituted benzenes—Priorities from Group A, p. 676, determine root name and substituents



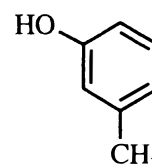
p-dibromobenzene
1,4-dibromobenzene



m-aminobenzoic acid
3-aminobenzoic acid

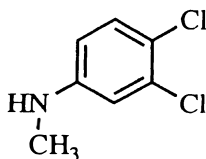


o-methoxybenzaldehyde
2-methoxybenzaldehyde

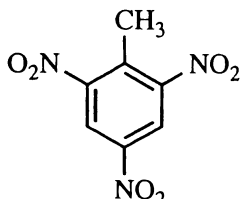


m-methylphenol
3-methylphenol

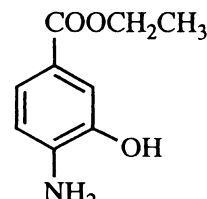
D. Polysubstituted Benzenes—must use numbers to indicate substituent position



3,4-dichloro-*N*-methylaniline



2,4,6-trinitrotoluene
(TNT)

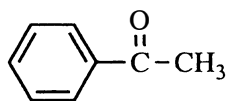


ethyl 4-amino-3-hydroxybenzoate

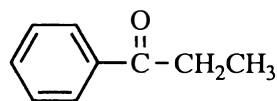
Appendix 1, Summary of IUPAC Nomenclature, continued

E. Aromatic Ketones

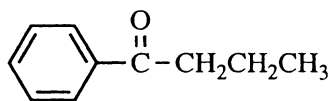
A special group of aromatic compounds are ketones where the carbonyl is attached to at least one benzene ring. Such compounds are named as "phenones", the prefix depending on the size and nature of the group on the other side of the carbonyl. These are the common examples:



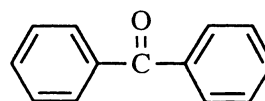
acetophenone



propiophenone



butyrophenone



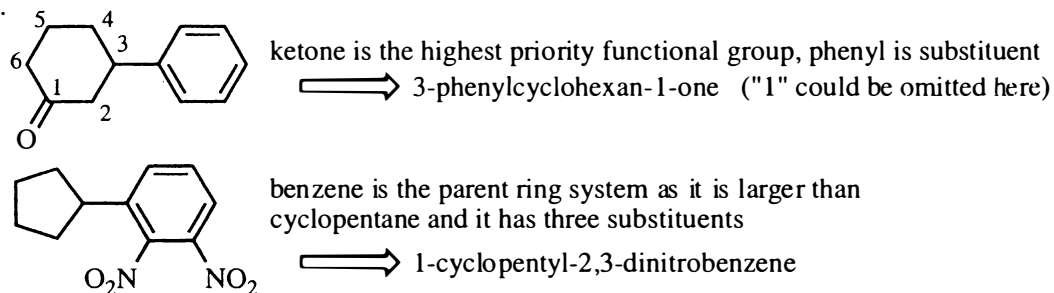
benzophenone

V. Nomenclature of Bicyclic Compounds

"Bicyclic" compounds are those that contain two rings. There are four possible arrangements of two rings that depend on how many atoms are shared by the two rings. The first arrangement in which the rings do not share any atoms does not use any special nomenclature, but the other types require a method to designate how the rings are put together. Once the ring system is named, then functional groups and substituents follow the standard rules described above.

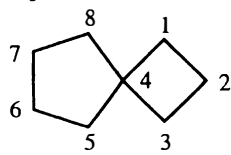
Type 1. Two rings with no common atoms

These follow the standard rules of choosing one parent ring system and describing the other ring as a substituent.

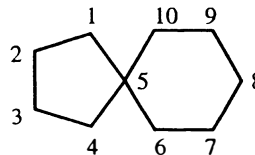


Type 2. Two rings with one common atom—spiro ring system

The ring system in spiro compounds is indicated by the word "spiro" (instead of "cyclo"), followed by brackets indicating how many atoms are contained in each path around the rings, ending with the alkane name describing how many carbons are in the ring systems including the spiro carbon. (If any atoms are not carbons, see section VI.) Numbering follows the smaller path first, passing through the spiro carbon and around the second ring.



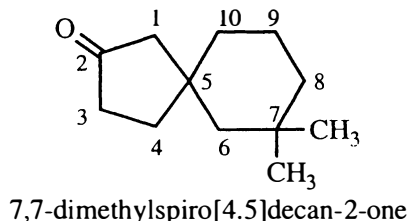
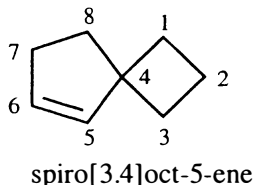
spiro[3.4]octane



spiro[4.5]decane

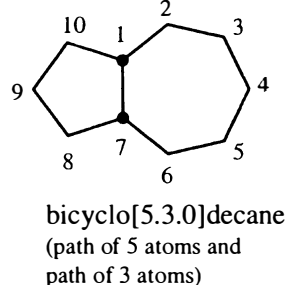
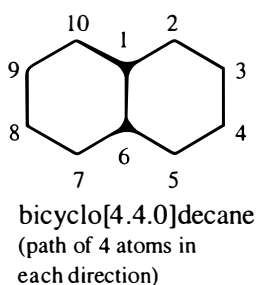
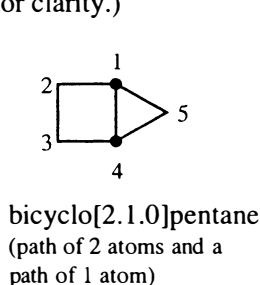
Appendix 1, Summary of IUPAC Nomenclature, continued

Substituents and functional groups are indicated in the usual ways. Spiro ring systems are always numbered smaller before larger, and numbered in such a way as to give the highest priority functional group the lower position number.



Type 3. Two rings with two common atom—fused ring system

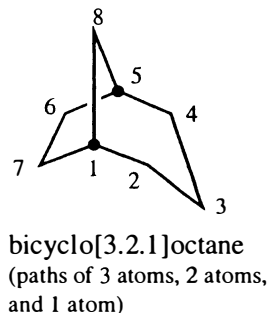
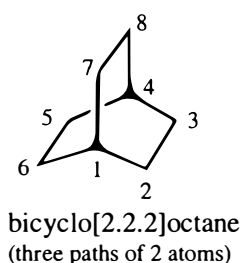
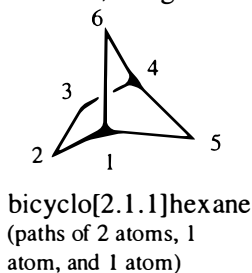
Two rings that share two common atoms are called fused rings. This ring system and the next type called bridged rings share the same designation of ring system. Each of the two common atoms is called a bridgehead atom, and there are three paths between the two bridgehead atoms. In contrast with naming the spiro rings, the *longer* path is counted first, then the shorter, then the shortest. In fused rings, the shortest path is always a zero, meaning zero atoms between the two bridgehead atoms. Numbering starts at a bridgehead, continues around the largest ring, through the other bridgehead and around the shorter ring. (In these structures, bridgeheads are marked with a dark circle for clarity.)



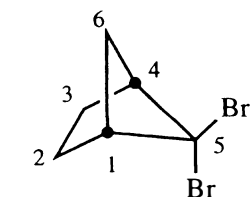
Substituents and functional groups are indicated in the usual ways. Fused rings systems are always numbered larger before smaller, and numbered in such a way as to give the highest priority functional group the lower position number.

Type 4. Two rings with more than two common atom—bridged ring system

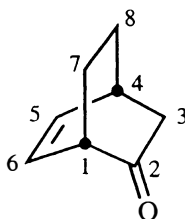
Two rings that share more than two common atoms are called bridged rings. Bridged rings share the same designation of ring system as Type 3 in which there are three paths between the two bridgehead atoms. The longer path is counted first, then the medium, then the shortest. Numbering starts at a bridgehead, continues around the largest ring, through the other bridgehead and around the medium path, ending with the shortest path numbered from the original bridgehead atom. (In these structures, bridgeheads are marked with a dark circle for clarity.)



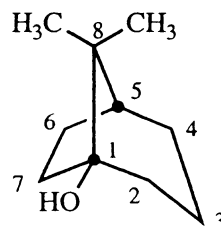
Appendix 1, Summary of IUPAC Nomenclature, continued



5,5-dibromo-
bicyclo[2.1.1]hexane



bicyclo[2.2.2]oct-5-en-2-one



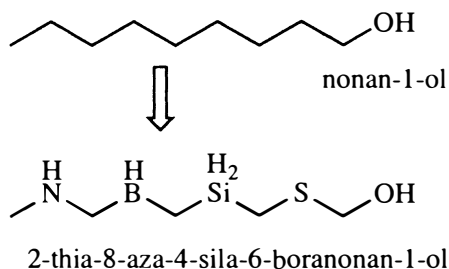
8,8-dimethyl-
bicyclo[3.2.1]octan-1-ol

VI. Replacement Nomenclature of Heteroatoms

The term "heteroatom" applies to any atom other than carbon or hydrogen. It is common for heteroatoms to appear in locations that are inconvenient to name following basic rules, so a simple system called "replacement nomenclature" has been devised. The fundamental principle is to name a compound as if it contained only carbons in the skeleton, plus any functional groups or substituents, and then indicate which carbons are "replaced" by heteroatoms. The prefixes used to indicate these substitutions are listed here *in decreasing priority and listed in this order in the name*:

Element	Prefix
O	oxa
S	thia
N	aza
P	phospha
Si	sil
B	bora

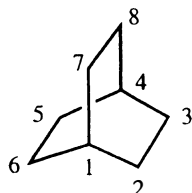
Example



In the above example, note that the (imaginary) compound no longer has nine carbons, even though the name still includes "nonan". The heteroatoms have replaced carbons, but the compound is named as if it still had those carbons.

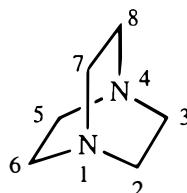
Where the replacement system is particularly useful is in polycyclic compounds. Shown below are three examples of commercially available and synthetically useful reagents that use this system.

parent hydrocarbon



bicyclo[2.2.2]octane

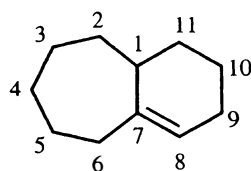
reagent



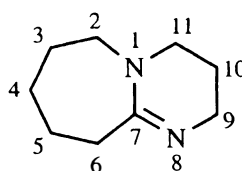
1,4-DiAzaBiCyclo[2.2.2]Octane
(upper case added to explain abbreviation)

abbreviation

DABCO



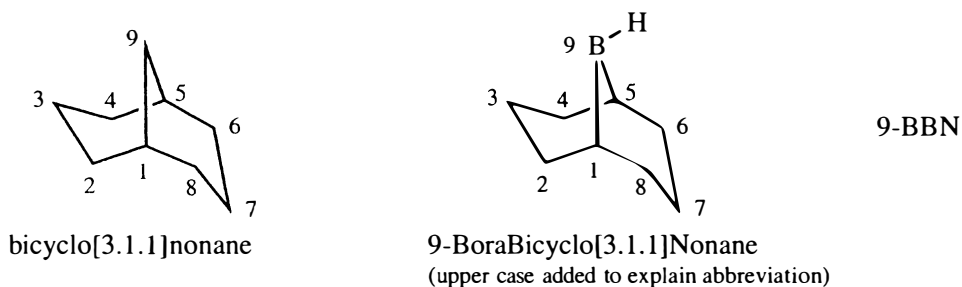
bicyclo[5.4.0]undec-7-ene



1,8-DiazaBicyclo[5.4.0]Undec-7-ene
(upper case added to explain abbreviation)

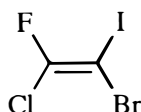
DBU

Appendix 1, Summary of IUPAC Nomenclature, continued

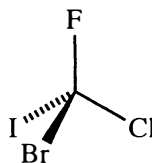


VII. Designation of Stereochemistry: Cahn-Ingold-Prelog system

Is this alkene cis or trans?

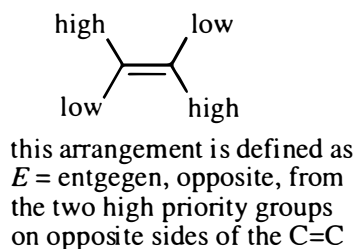
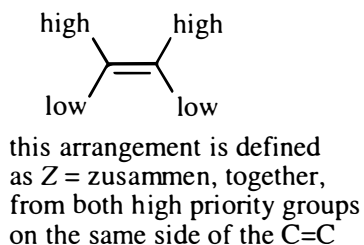


How can we distinguish this structure from its mirror image?

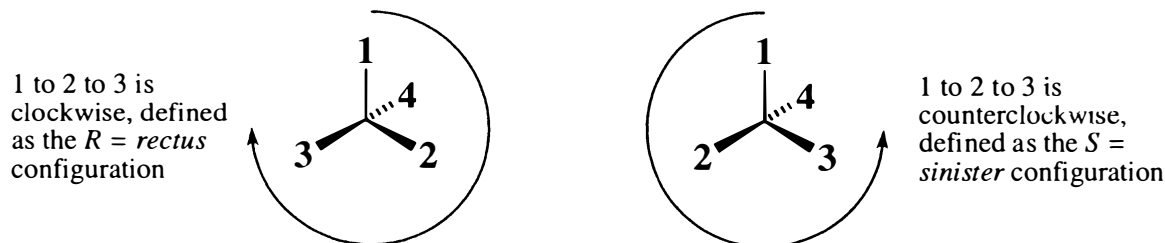


Compounds that exhibit stereoisomerism, whether geometric isomers around double bonds, substituent groups on rings, or molecules with asymmetric tetrahedral atoms (which are almost always carbons), require a system to designate relative and absolute orientation of the groups. The terms *cis/trans*, *D/L* in carbohydrates and amino acids, and *d/l* for optically active compounds, are limited and cannot be used generally, although each still is used in appropriate situations. For example, *cis/trans* still is used to indicate relative positions of substituents around a ring.

A system developed by chemists Cahn, Ingold, and Prelog, uses a series of steps to determine group priorities, and a definition of position based on the relative arrangement of the groups. In alkenes, the system is relatively simple:



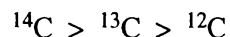
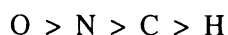
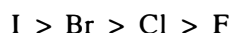
As with alkenes, the orientation around an asymmetric carbon can be only one of two choices. In three dimensions, clockwise and counterclockwise are the only two directions that are definite, and even that description requires a fixed reference point. To designate configuration, the lowest (fourth) priority group is always placed farthest away from the viewer (indicated by a dashed line), and the group priorities will follow 1 to 2 to 3 in either a clockwise or a counterclockwise direction.



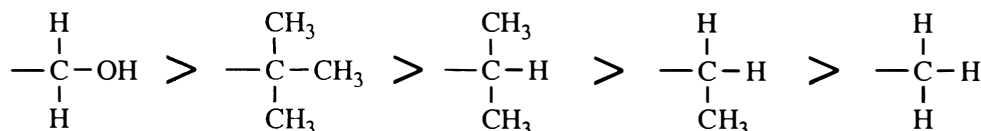
Appendix 1, Summary of IUPAC Nomenclature, continued

The only step remaining is to determine the priority of groups, for which there is a carefully defined set of rules.

Rule 1. Consider the first atom of the group, the point of attachment. Atoms with higher atomic number receive higher priority. Heavier isotopes have higher priority than lighter isotopes.

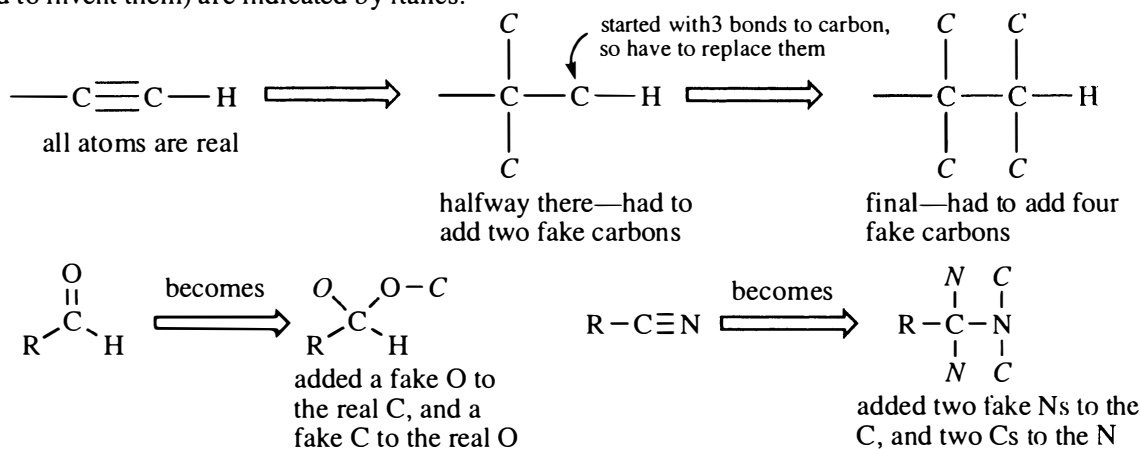


Rule 2. If the first atoms of two or more groups are the same, go out to the next atoms to break the tie. One high priority atom takes priority over any number of lower-priority atoms.

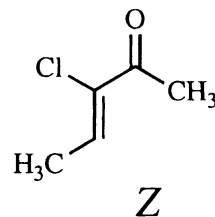
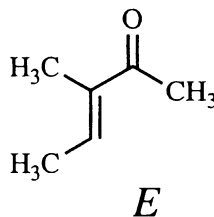
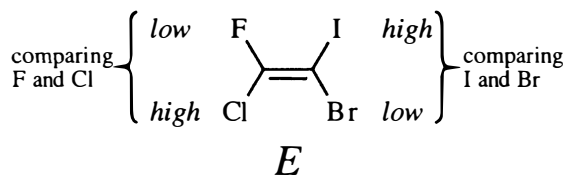


Rule 3. Treat multiple bonds as if they were all single bonds; one will be to the real atom, the others will be to imaginary atoms.

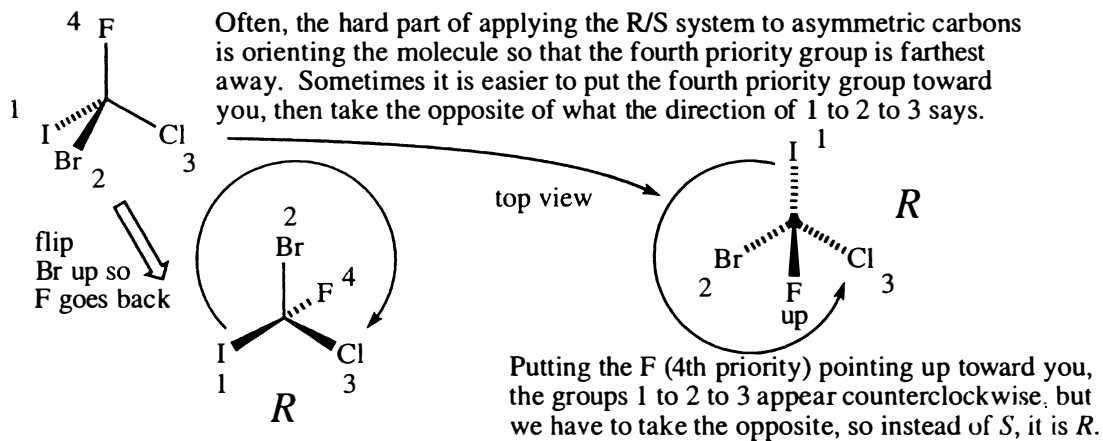
This is the hardest rule to put into practice. This example of an alkyne shows stepwise how to accomplish this. In the pictures, imaginary atoms (ones that did not start out in the structure, we had to invent them) are indicated by italics.



Examples applying the Cahn-Ingold-Prelog system



Appendix 1, Summary of IUPAC Nomenclature, continued

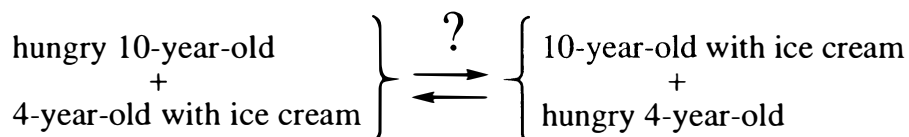


Appendix 2: Summary of Acidity and Basicity

Imagine that you are at a family reunion where you can observe the competition for ice cream cones among your nieces and nephews. Pretty soon, you formulate a generalization: the older kids can hold onto their ice cream cones more strongly than the younger ones. Another way of saying it is that the older ones are less likely to give up their cones. You could even represent this information in a table showing a series of equilibria between the child with ice cream, and the free ice cream plus the hungry child. The differences in strength could also be quantitated: the larger the hunger factor, pK_H , the less likely the child will give up the ice cream.

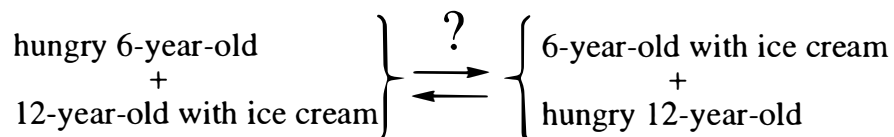
<u>pK_H</u>	<u>Approximate pK_H Values of Children</u>		
12	12-year-old with ice cream	$\rightleftharpoons$	ice cream + hungry 12-year-old
10	10-year-old with ice cream	$\rightleftharpoons$	ice cream + hungry 10-year-old
8	8-year-old with ice cream	$\rightleftharpoons$	ice cream + hungry 8-year-old
6	6-year-old with ice cream	$\rightleftharpoons$	ice cream + hungry 6-year-old
4	4-year-old with ice cream	$\rightleftharpoons$	ice cream + hungry 4-year-old

What good is this table? It allows anyone to make predictions about what will happen when kids with ice cream are mixed with hungry kids.



If the hungry 10-year-old was left unattended in a room with the 4-year-old with ice cream, which side of this equilibrium would be favored when you came back in a few minutes: "reactants" or "products"? More likely than not, there would be an ice cream transfer in your absence; "products" would be favored. You could have predicted this from the table, and you could generalize: the hungry 10-year-old will be strong enough to rip the ice cream away from any kid lower on the table than the 10-year-old him/herself.

Let's predict the results of another equilibrium:



Is the hungry 6-year-old strong enough to pull the ice cream away from the 12-year-old? Not in most families. The table shows that the only chance for the hungry 6-year-old is to find a 4-year-old with ice cream. The 12-year-old with ice cream is pretty safe as long as the hunger table doesn't go to higher ages.

If you understand this analogy and can make predictions of ice cream transfer using the table, then you can understand how to predict the direction of equilibrium in acid-base reactions. Turn the page.

Appendix 2 continued, Summary of Acidity and Basicity

To set the stage

A few generalizations:

A) This Appendix deals with protic acids and bases, called Bronsted-Lowry acids. Similar statements can be made about Lewis acids but they are not the focus of this discussion.

B) Values of pK_a are measures of equilibrium constants, described further below. Values between 0 and 15.7 are measured by titration in water solution and are known accurately, to within 0.1 pK unit and sometimes better. Values outside of this range cannot be measured in water because of the leveling effect of water, and there is no universally accepted method for measuring these pK_a values. This lack of a single standard of measurement means that the values below 0 and above 15.7 should be considered relative, not absolute. If your instructor says the pK_a of methane is 46 and this book says it is 50, those should be considered the same value within experimental variation.

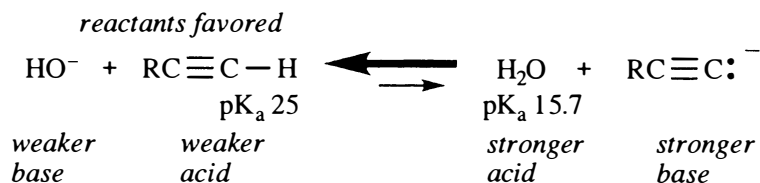
C) Acidity is a thermodynamic property, and the acid equilibrium constant, K_a , is a measure of the relative concentrations of species in the protonated and unprotonated form. As most organic acids are weak acids, meaning they are present mostly in the protonated form at equilibrium, the $K_a < 1$. Since the $pK_a = -\log K_a$, the pK_a values will be greater than 0, with the larger pK_a representing a weaker acid. If this is not clear, review text section 1-13.

D) Acids do not spontaneously spit out a proton! Despite our way of writing ionization equilibria as shown on the next page, acids do not give up a proton unless a base comes by to take the proton away. The reactions as drawn in the table should be considered half-reactions, just as the reactions in the electromotive series were half-reactions for balancing oxidation-reduction reactions in general chemistry.

I. Predicting equilibrium position

Look at the table on p. 691 and notice how it looks just like the "children-with-ice-cream" table. We can use this table to make predictions about equilibrium position in acid-base reactions just as we did for the children with ice cream.

1) *A base will deprotonate any acid stronger than its conjugate acid.* This is the most important principle of predicting acid-base reactions. On the table, this means that any base, hydroxide for example, can react with any acid more acidic than the conjugate acid of itself, water in our example. So hydroxide is a strong enough base to pull the proton from any of these: bicarbonate ion, a phenol, carbonic acid, a carboxylic acid, or a sulfonic acid. We can also predict that hydroxide is NOT a strong enough base to react with any acid above water on the table; for example, a mixture of hydroxide with an alkyne will favor the reactants at equilibrium, with only a small amount of products.



2) Another way of predicting the position of an equilibrium is to assign "stronger" and "weaker" to the acid and base on each side of the equation, using the table to determine which is stronger and which is weaker. *Equilibrium will always favor the weaker acid and base.* This method will always give the same answer as the principle in #1 above.

To lead into the next section, look again at the table on p. 691 and notice two things: a) with only a couple of exceptions, all the acidic protons are on either oxygen or carbon; and b) generalizations can be made about the acidity of functional groups. Learning to correlate acidity with functional group is important in predicting reactivity of the functional group.

Appendix 2 continued, Summary of Acidity and Basicity

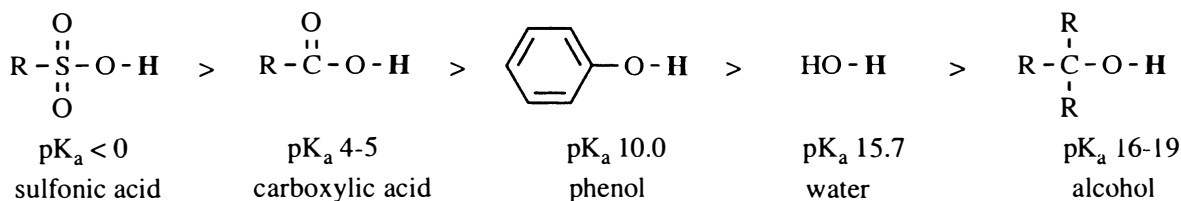
Approximate pKa Values of Organic Compounds

		pKa				
<i>weaker acid</i>	alkane	≈ 50	$\text{R}-\overset{\text{ }}{\underset{\text{ }}{\text{C}}}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{R}-\overset{\text{ }}{\underset{\text{ }}{\text{C}}}^-$	<i>stronger base</i>
	alkene	≈ 45	$=\text{C}-\overset{\text{\'/}}{\underset{\text{H}}{\text{C}}}$	$\rightleftharpoons$	$\text{H}^+ + =\text{C}-\overset{\text{\'/}}{\underset{\text{\'/}}{\text{C}}}^-$	
	amine	35-40	$-\ddot{\text{N}}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + -\ddot{\text{N}}^-$	
		≈ 35	$\text{H}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{H}^-$	
	alkyne	≈ 25	$\text{RC}\equiv\text{C}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{RC}\equiv\text{C}^-$	
	ketone and ester	20-25	$-\overset{\text{O}}{\parallel}\text{C}-\overset{\text{ }}{\underset{\text{ }}{\text{C}}}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + -\overset{\text{O}}{\parallel}\text{C}-\overset{\text{ }}{\underset{\text{ }}{\text{C}}}^-$	
	alcohol	≈ 18	$\text{R}-\overset{\text{R}}{\underset{\text{R}}{\text{C}}}-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{R}-\overset{\text{R}}{\underset{\text{R}}{\text{C}}}-\ddot{\text{O}}^-$	
		≈ 17	$\text{R}-\overset{\text{H}}{\underset{\text{R}}{\text{C}}}-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{R}-\overset{\text{H}}{\underset{\text{R}}{\text{C}}}-\ddot{\text{O}}^-$	
		≈ 16	$\text{R}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{R}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\ddot{\text{O}}^-$	
↑ cannot be measured in water solution						
		15.7	H_2O	$\rightleftharpoons$	$\text{H}^+ + \text{HO}^-$	
↓ measured in water solution						
		10.3	HCO_3^-	$\rightleftharpoons$	$\text{H}^+ + \text{CO}_3^{2-}$	
	phenol	≈ 10	$\text{Ar}-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{Ar}-\ddot{\text{O}}^-$	
		6.4	H_2CO_3	$\rightleftharpoons$	$\text{H}^+ + \text{HCO}_3^-$	
	carboxylic acid	4-5	$\text{R}-\overset{\text{O}}{\parallel}\text{C}-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{R}-\overset{\text{O}}{\parallel}\text{C}-\ddot{\text{O}}^-$	
<i>stronger acid</i>	sulfonic acid	< 0	$\text{RSO}_2-\text{O}-\text{H}$	$\rightleftharpoons$	$\text{H}^+ + \text{RSO}_2-\ddot{\text{O}}^-$	<i>weaker base</i>

Appendix 2 continued, Summary of Acidity and Basicity

II. Correlation of Acidity with Functional Group

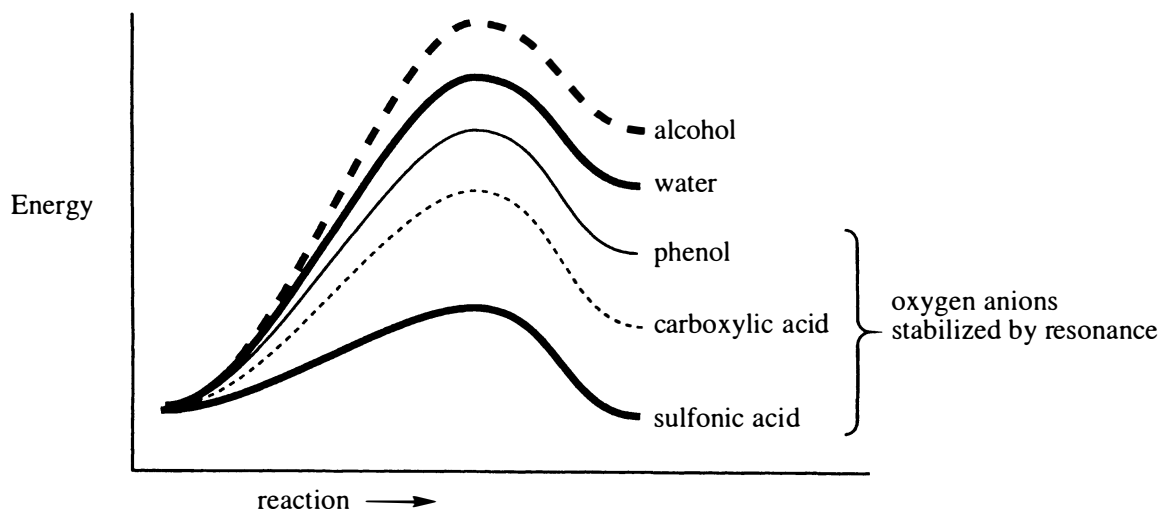
A. Oxygen Acids



Sulfonic acids are the strongest of the oxygen acids but are not common in organic chemistry. Carboxylic acids, however, are everywhere and are considered the strongest of the common organic oxygen acids. (Note that "strong" and "weak" are relative terms: acetic acid, pK_a 4.74, was a "weak" acid in general chemistry in comparison to sulfuric and hydrochloric acids, but acetic acid is a "strong" acid in organic chemistry relative to the other oxygen acids.) Phenols having OH groups on benzene or other aromatic rings are still stronger acids than water.

Why are phenols, carboxylic acids, and sulfonic acids stronger acids than water? Because their anions are stabilized by resonance. (Refer to text sections 1-13, 10-6, and 20-4, especially Figure 20-1.) Let's look at that statement in more detail.

Remember that acidity is a thermodynamic property; that is, acidity equilibrium depends on the difference in energy between the reactants and products. The more the anion is stabilized by resonance, the lower in energy it is, and the less positive the ΔG , as shown on the reaction energy diagram:



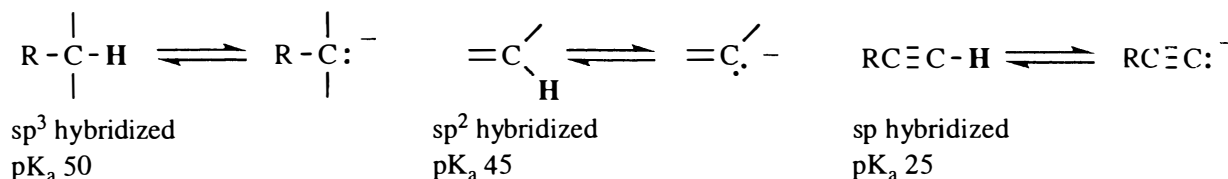
Why are alcohols weaker acids than water? There are two effects that contribute, both of which are consistent with the trend that 1° alcohols (pK_a 16) are slightly stronger than 2° alcohols (pK_a 17) which are slightly stronger than 3° alcohols (pK_a 18). Alkyl groups are mildly electron-donating in their inductive effect (more about this later) and destabilize the anion, as shown in the energy diagram above. Second, the more crowded the anion is, the less it can be stabilized by hydrogen bonding with the solvent.

Appendix 2 continued, Summary of Acidity and Basicity

B. Carbon Acids

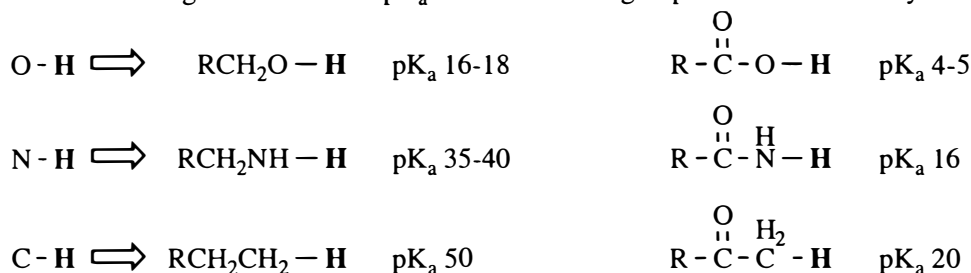
When we think of "acids", we do not usually think of protons on carbon, yet carbon acids and the carbanions that come from them are of tremendous importance in organic chemistry.

"Unstabilized" carbon acids are those that do not have any substituent to stabilize the anion. Alkanes, with only sp^3 carbons are the weakest acids with pK_a around 50. The vinyl carbon in a carbon-carbon double bond is sp^2 hybridized with the electrons of the anion slightly closer to the positive nucleus, leading to some stabilization of the anion. This type of stabilization is particularly important in alkynes with sp hybridized carbons.



C. Carbon Acids Alpha to Carbonyl (This topic is described in detail in text section 22-2B.)

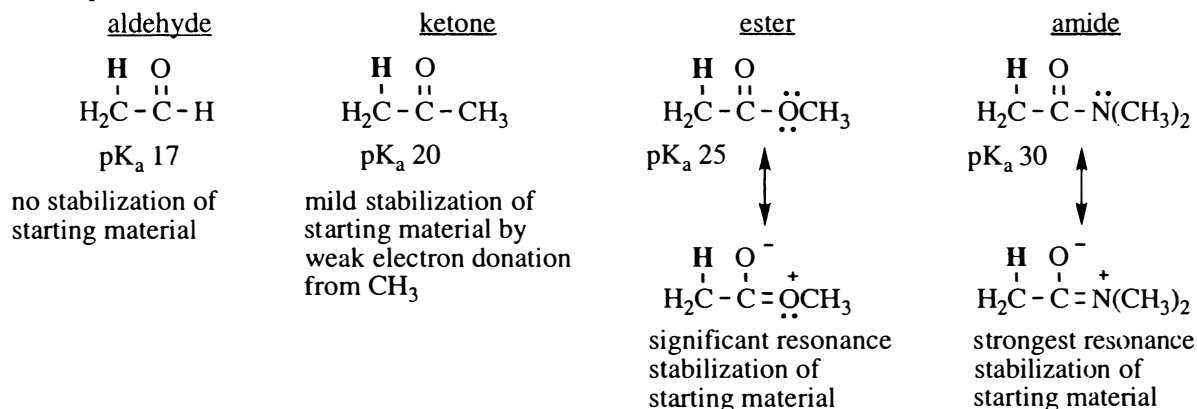
Look at these huge differences in pK_a when the acidic group is next to a carbonyl.



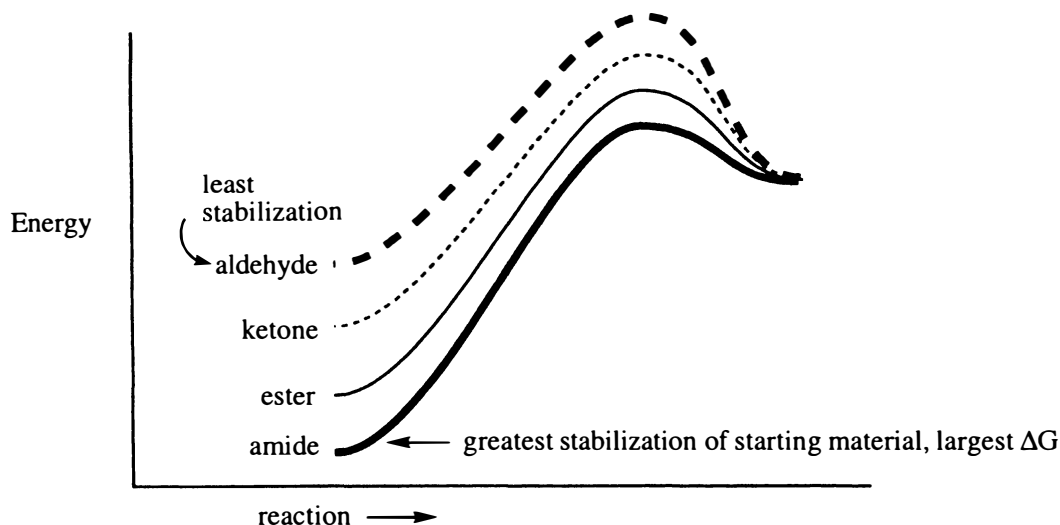
Hydrogens alpha to carbonyl are unusually acidic because of resonance stabilization of the anionic conjugate base.

D. Acidities of Acyl Functional Groups

In addition to the significant variation in the acidity of alpha hydrogens depending on which atom the H is bonded to, what is on the other side of the carbonyl also has a dramatic influence. In this case, the stabilization is more important on the starting material, not on the conjugate base. See the energy diagram on p. 694.

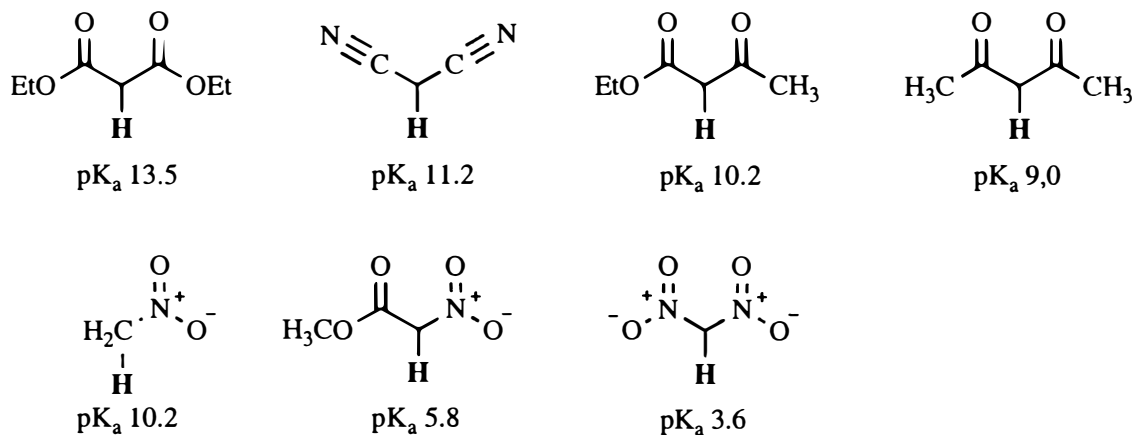


Appendix 2 continued, Summary of Acidity and Basicity



E. Carbon Acids Between Two Carbonyls (This topic is described in detail in text section 22-15.)

While a hydrogen alpha to one carbonyl moves into the pK_a 20-25 range for ketones and esters respectively, a hydrogen between two carbonyls (cyano and nitro are similar to carbonyl electronically) is more acidic than water. The increased resonance stabilization of the conjugate base is largely responsible, but there are subtle variations depending on the type of functional group as noted at the bottom of p. 693. Look at the enormous influence of the nitro group.



III. Correlation of Basicity with Functional Group

The bulk of this Appendix is on acidity because many more functional groups are acidic than are basic. Basically (oooh, sorry), only one functional group is basic: amines. There is variation among aliphatic, aromatic, and heteroaromatic amines; these are covered thoroughly in text sections 19-5 and 19-6. One point in the text, just before Table 19-3, deserves emphasis: for any conjugate acid-base pair:

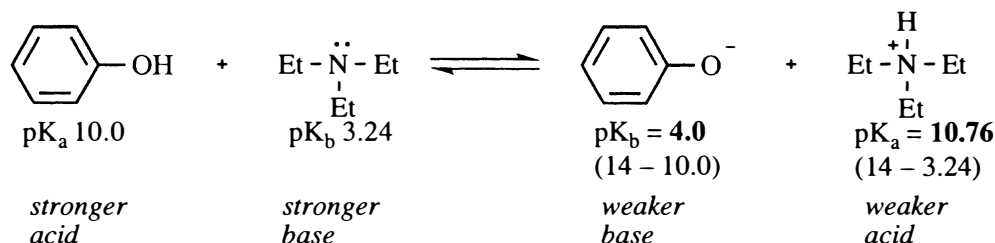
$$pK_a + pK_b = 14$$

Appendix 2 continued, Summary of Acidity and Basicity

This simple algebraic relationship is very useful:

Sample problem. Is triethylamine (pK_b 3.24) a strong enough base to deprotonate phenol (pK_a 10.0)?

We need to calculate either the pK_a of the conjugate acid of triethylamine or the pK_b of the conjugate base of phenol to see which is stronger and weaker. Then we can say with certainty which side of the equilibrium will be favored.



Aha! Products are favored at equilibrium, so the correct answer to the question is "Yes, triethylamine is a strong enough base to deprotonate phenol."

Try this for fun: How weak must a base be before it does NOT deprotonate phenol? What algebraic rule can you formulate to predict whether any combination of acid and base will favor products or reactants?

IV. Substituent Effects on Acidity

So far, we have focused on acidities of different functional groups. Let's turn to more minor, more subtle, structural changes to see what effect substituents will have on the acidity of a group. Primarily, we imply *electronic* effects as opposed to *steric* effects, but this Appendix will conclude with a discussion of how steric and electronic effects can work together.

A. Classification of Substituents—Induction and Resonance

Substituent groups can exert an electronic effect on an acidic functional group in two different ways: through sigma bonds, where this is called an *inductive effect*, or through p orbitals and pi bonds which is called a *resonance effect*. Groups can also be electron-donating or electron-withdrawing by either of the mechanisms, so there are four possible categories for groups. Note that a group can appear in more than one category, even in conflicting groups!

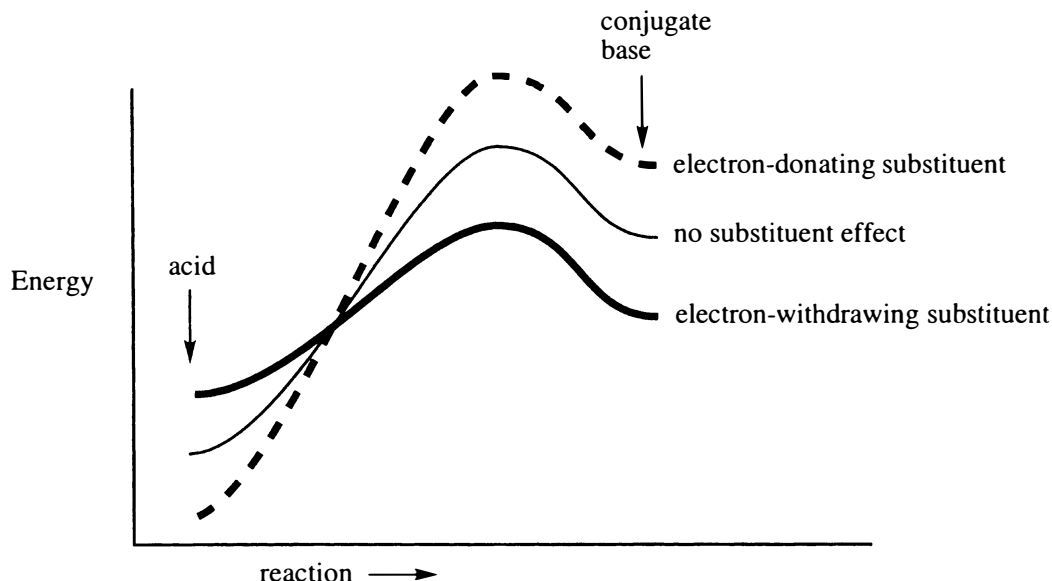
- a) Electron-donating by induction: only alkyl groups (abbreviated R) have electrons to share by induction;
- b) Electron-withdrawing by induction: every group that has a more electronegative atom than carbon is in this category; some examples: F, Cl, Br, I, OH, OR, NH_2 , NHR, NR_2 , NO_2 , $C=O$, CN, SO_3H , CX_3 where X is halogen;
- c) Electron-donating by resonance: groups that have electron pairs to share: F, Cl, Br, I, OH, OR, NH_2 , NHR, NR_2 ;
- d) Electron-withdrawing by resonance: NO_2 , $C=O$, CN, SO_3H .

Appendix 2 continued, Summary of Acidity and Basicity

B. Generalizations on Electronic Effects on Acidity (refer to text section 20-4B)

Electric charge is the key to understanding substituent effects. An acid is always more positive than its conjugate base; in other words, the conjugate base is always more negative than the acid. Electron-donating and electron-withdrawing groups will have opposite effects on the acid-base conjugate pair.

Electron-donating groups stabilize the more positive acid form and destabilize the more negative conjugate base. From the diagram, it is apparent that electron-donating groups widen the energy gap between reactants and products, making ΔG more positive, favoring reactants more than products. In essence, this weakens the acid strength.



Electron-withdrawing groups destabilize the more positive acid form and stabilize the more negative conjugate base, narrowing the energy gap between reactants and products, making ΔG less positive. Products are increased in concentration at equilibrium which we define as a stronger acid.

Electron-withdrawing groups increase acid strength; electron-donating groups decrease acid strength.

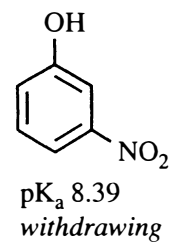
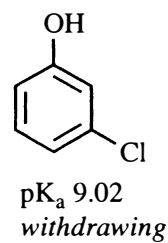
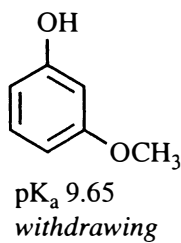
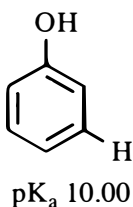
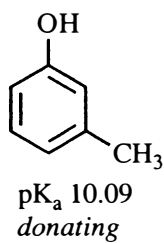
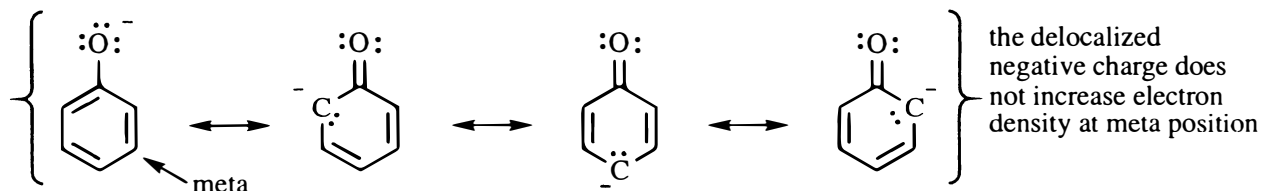
C. Inductive Effects on Acidity

Text section 20-4B gives a thorough explanation of the inductive effect of electron-withdrawing groups on simple carboxylic acids, from which three generalizations arise:

- A) Acidity increases with stronger electron-withdrawing groups. (See problem 20-33.)
- B) Acidity increases with greater number of electron-withdrawing groups.
- C) Acidity increases with closer proximity of the electron-withdrawing group to the acidic group.

We don't usually look to aromatic systems for examples of inductive effects, because the pi system of electrons is ripe for resonance effects. However, in analyzing the resonance forms of phenoxide on the next page, it becomes apparent that the negative charge is never distributed on the meta carbons. Meta substituents cannot exert any resonance stabilization or destabilization; at the meta position, substituents can exert only an inductive effect. The series of phenols demonstrates this phenomenon, consistent with aliphatic carboxylic acids.

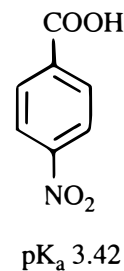
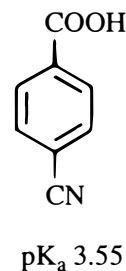
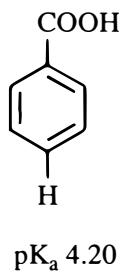
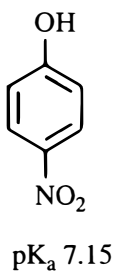
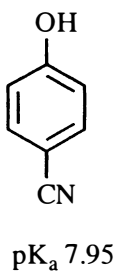
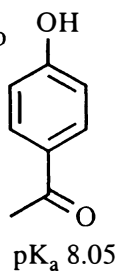
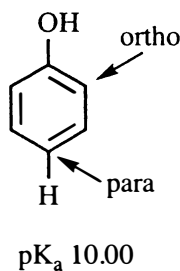
Appendix 2 continued, Summary of Acidity and Basicity



D. Resonance Effects on Acidity—benzoic acids and phenols (review the solution to problem 20-45)

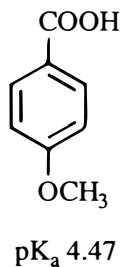
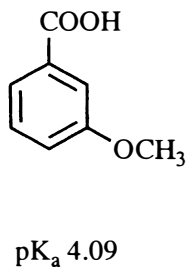
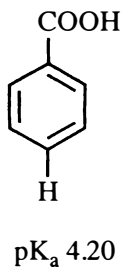
Resonance effects can be expressed with placement of substituents at ortho or para positions, but ortho has the complication of steric effects, so just para substitution is shown here.

Electron-withdrawing substituents increase the acidity of benzoic acids and phenols:



Electron-donating by resonance but electron-withdrawing by induction:

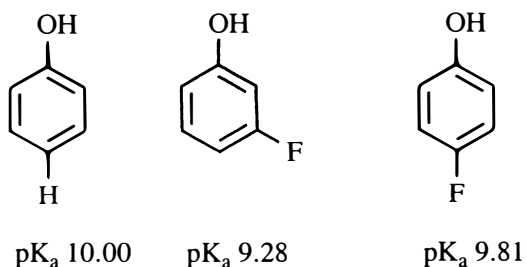
There is a group of substituents that donate by resonance but withdraw by induction: alkoxy groups and halogens are the most notable examples, and the acidity data provide an insight into which effect is stronger.



meta-Methoxybenzoic acid is stronger than benzoic acid, consistent with electron-withdrawing by induction which is expressed at the meta position. But the para isomer is *weaker* than benzoic acid; electron donation by resonance has not only compensated for the inductive effect (which is still operative at the para position) but has decreased the acidity even further. Thus, the donating effect by resonance must be stronger than the withdrawing effect by induction for the methoxy group.

See another example on the next page.

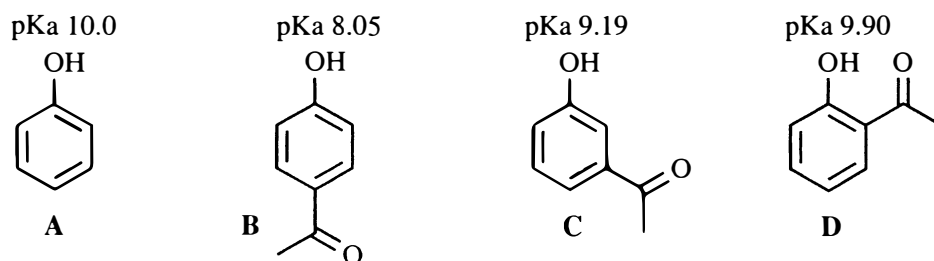
Appendix 2 continued, Summary of Acidity and Basicity



meta-Fluorophenol is stronger than phenol, consistent with electron-withdrawing by induction which is expressed at the meta position. The para isomer is still stronger than phenol; electron donation by resonance has not compensated for the inductive effect (which is still operative at the para position). Thus, the donating effect by resonance must be weaker than the withdrawing effect by induction for the fluoro group.

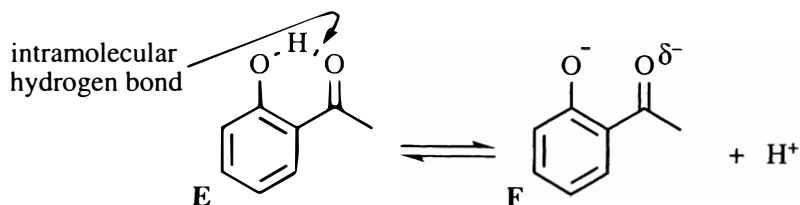
Studying substituent effects on acidity is the standard method of determining whether a group is donating or withdrawing by induction and resonance.

E. Proximity Effects of Substituents

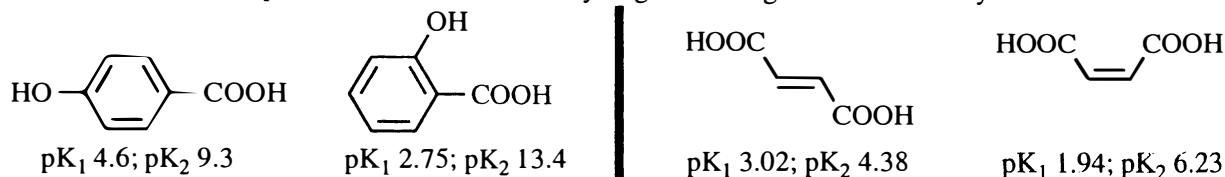


Three effects influence the pK_a values of these substituted phenols. In C, the acetyl group at the meta position is electron-withdrawing by induction only. In B, the acetyl group at the para position exerts both resonance and inductive effects, both of which are electron-withdrawing, making the acid stronger. In theory, substituents at the ortho position should be like para, exerting both resonance and inductive effects; in fact, the inductive effect should be stronger because of closer proximity to the acidic group. So we would predict D to be a stronger acid than B, yet it is not. What other effect is operating?

Structure E shows that because of the proximity of the acetyl group to the OH, *intramolecular hydrogen bonding* is possible. Hydrogen bonding stabilizes the starting material, lowering the energy of the starting material and making ΔG more positive. Intuitively, it should be apparent that a hydrogen held between two oxygens will be more difficult to remove by a base. Also, after the proton has left as shown in structure F, the negative charge on the phenolic oxygen is close to the partial negative charge on the oxygen of the carbonyl, destabilizing product F, raising its energy, also making ΔG more positive. The proximity of the acetyl group influences both sides of the equation to make the acid weaker.



Here are two more examples where intramolecular hydrogen-bonding influences acidity.

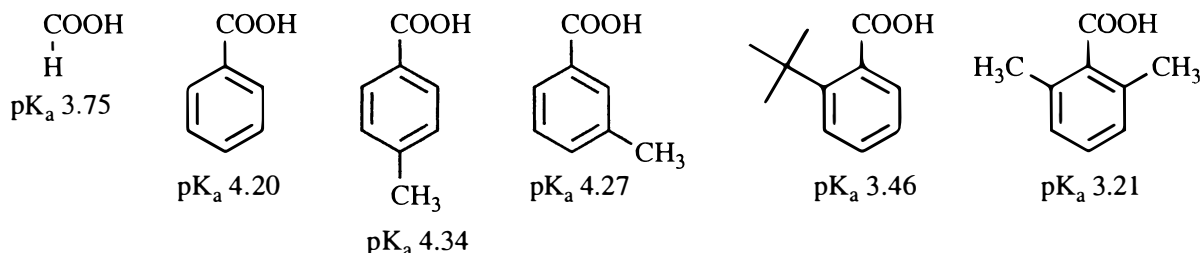


Appendix 2 continued, Summary of Acidity and Basicity

F. Steric Inhibition of Resonance

Another type of proximity effect arises when the placement of a substituent interferes with the orbital overlap required for resonance stabilization. This can be seen clearly in the acidity of substituted benzoic acids and in the basicity of substituted anilines.

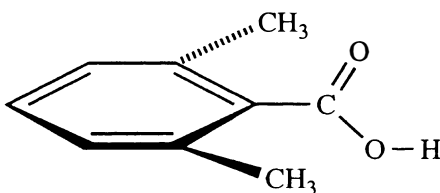
Let's analyze this series of carboxylic acids.



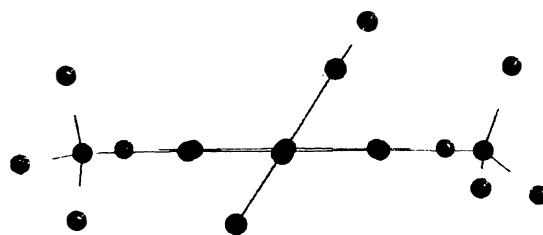
Formic acid, pK_a 3.75, serves as the reference carboxylic acid. Benzoic acid is weaker because the phenyl group is electron-donating by resonance, stabilizing the protonated form. Methyl substituents are known to be electron-donating by induction, strengthening the electron-donating effect, making the meta- and para-substituted acids weaker than benzoic acid.

Then come the anomalies. Alkyl groups are electron-donating by induction and should weaken the acids, but the ortho-t-butyl and the 2,6-dimethylbenzoic acids are not only stronger than benzoic acid, they are stronger than formic acid! Something has happened to turn the phenyl group into an electron-withdrawing group.

Phenyl is electron-donating by resonance but electron-withdrawing by induction, so what has happened is that the ortho substituents have forced the COOH out of the plane of the benzene ring so that there is no resonance overlap between the benzene ring and the COOH orbitals. The COOH "feels" the benzene ring as simply an inductive substituent. Resonance has been "inhibited" because of the steric effect of the substituent.

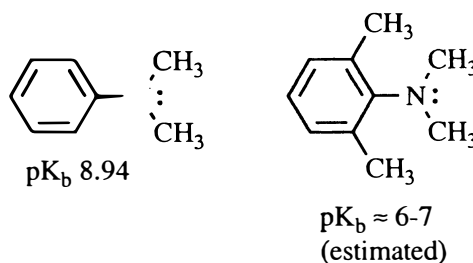


COOH group is not parallel with the plane of the benzene ring—no resonance interaction.



this three-dimensional view down the C-C bond between the COOH and the benzene ring shows that COOH is twisted out of the benzene plane

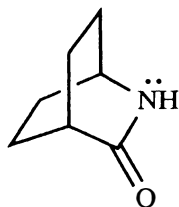
The same phenomenon is observed in substituted anilines. Anilines are usually much weaker bases than aliphatic amines because of resonance overlap of the nitrogen's lone pair of electrons with the pi system of benzene. When that resonance is disrupted, the aniline becomes closer in basicity to an aliphatic amine. (See problem 19-49(c).)



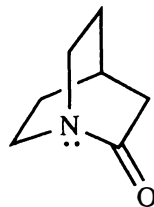
More examples on the next page.

Appendix 2 continued, Summary of Acidity and Basicity

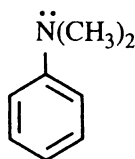
Examples of steric inhibition of resonance:



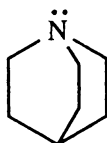
amide—not basic because of resonance sharing of N lone pair with carbonyl



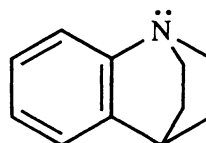
strong base similar to aliphatic amine; geometry of bridged ring prevents overlap of N lone pair with carbonyl



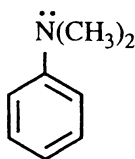
pK_b 8.9
3° aromatic amine



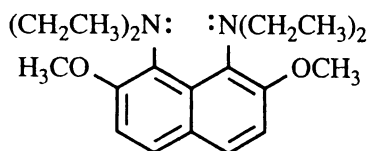
pK_b 3.4
3° aliphatic amine



pK_b 6.2
3° amine, and the N is bonded to a benzene, but the bridged ring system prevents overlap of N lone pair with benzene



pK_b 8.9



pK_b - 2.3 (yes, negative!)

Not only is steric inhibition of resonance important in this example, but so is intramolecular hydrogen-bonding in the protonated form. Draw a picture.